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Special Article

THE USEFULNESS OF USELESS KNOWLEDGE

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EDITOR'S NOTE.—*This paper, now nearly twenty years old, is republisned with the permission of Dr. Flexner. With some textual changes, it was delivered as a Commencement Address at Bryn Mawr College on June 2, 1937, and was first published in the Bryn Mawr Alumnae Bulletin in July, 1937.*

On Oct. 11, 1938, Dr. Flexner presented it as an address on the occasion of the opening of the Squibb Institute for Medical Research; it was republished as a part of the Proceedings of that occasion.

The Editor of this JOURNAL *believes that Dr. Flexner's paper is one of those timeless contributions to scientific literature which deserves far wider dissemination than it has so far had, and especially among physicians interested in chronic illness.*

One needs only to recall that apparently useless (at the time) knowledge furnished by von Mering and Minkowski in 1889 led to the eventual conquest of diabetes; by Fleming in 1928 to the antibiotic era and the practical control of microbial infectious disease; and a host of other similar victories the path to which was laid by careful workers, themselves then unaware of the far-reaching implications of their seemingly impractical work. The major unsolved problems of chronic illness—cancer, atherosclerosis, essential hypertension, some forms of mental disease and many others—may well reach solution in similar fashion.

Permission to reprint has also been given by Dr. W. A. Feirer, the present Director of the Squibb Institute for Medical Research, and by the Editor, Bryn Mawr Alumnae Bulletin.

IT IS a strange contradiction that in the midst of a world torn by irrational hatreds that threaten civilization itself we are this afternoon dedicating this Institute and the services of devoted young men and women to the extension of knowledge, to the cure of disease, and to the amelioration of suffering. Life has never been logical—neither the life of nations nor the life of individuals. It is perhaps fortunate that illogicality can do something to rationalize and beautify human existence.

I shall speak to you for a few moments on a few aspects of irrationalism, for surely it is an irrational fact that it so often happens that the ceaseless quest for the useless should—sometimes soon and sometimes later—result in conferring some great practical boon upon harassed and floundering mankind. It is said with tiresome iteration that ours is a materialistic age and that its main concern should be the wider distribution of material goods and worldly opportunities. Let us accept this point of view. To whom shall we go for this nearer approach to the millennium? Not assuredly to those who are primarily engaged in the manufacture of goods or in the creation of concrete opportunities. The men and women who are today making the largest contribution to human happiness and human health are the quiet workers in laboratories and libraries and who in the pursuit of a devoted career do not pause to ask themselves, "what is the use?"

I recall a conversation which I had some years ago with Mr. George Eastman on the subject of use. Mr. Eastman, a wise and gentle, far-seeing man, gifted with exquisite taste in music and art, had been saying to me that he meant to devote his vast fortune to the promotion of education in useful subjects. I ventured to ask him whom he regarded as the most useful worker in science in the world. He replied instantaneously, "Marconi." I surprised him by saying: "Whatever pleasure we derive from the radio or however wireless and the radio may have added to human life, Marconi's share was practically negligible."

I shall not forget his astonishment on this occasion. He asked me to explain. I replied to him:

"Mr. Eastman, Marconi was inevitable. The real credit for everything that has been done in the field of wireless belongs, as far as such fundamental credit can be definitely assigned to anyone, to Professor Clerk Maxwell, who in 1865 carried out certain abstruse and remote calculations in the field of magnetism and electricity. Maxwell reproducted his abstract equations in a treatise published in 1873. Other discoveries supplemented Maxwell's theoretical work during the next fifteen years. Finally in 1887 and 1888 the scientific problem still remaining—the detection and demonstration of the electromagnetic waves which are the carriers of wireless signals—was solved by Heinrich Hertz, a worker in Helmholtz's laboratory in Berlin. Neither Maxwell nor Hertz had any concern about the utility of their work; no such thought ever entered their minds. They had no practical objective. The inventor in the legal sense was of course Marconi, but what did Marconi invent? Merely the last technical detail, the now obsolete receiving device called a coherer, almost universally discarded."

Hertz and Maxwell invented nothing, but it was their apparently useless theoretical work which was seized upon by a clever technician and which has created new means of communication, utility, and amusement by which men whose merits are relatively slight have obtained fame and earned millions. Who were the fundamentally useful men? Not Marconi, but Clerk Maxwell and Heinrich Hertz. Hertz and Maxwell were geniuses without thought of use. Marconi was a clever inventor with no thought but use.

The mention of Hertz's name recalled to Mr. Eastman the Hertzian waves, and I suggested that he might ask the physicists of the University of Rochester

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precisely what Hertz and Maxwell had done; but one thing I said he could be sure of, namely, that they had done their work without thought of use and that throughout the whole history of science most of the really great discoveries which had ultimately proved to be beneficial to mankind had been made by men and women who were driven, not by the desire to be useful, but merely by the desire to satisfy their curosity.

"Curiosity?", asked Mr. Eastman.

"Yes," I replied, "curiosity, which may or may not eventuate in something useful is probably the outstanding characteristic of modern thinking. It is not new. It goes back to Galileo, Bacon, Sir Isaac Newton, and to the Greeks, and it must be absolutely unhampered. Institutions of learning and institutions of research should be devoted to the cultivation of curiosity and the less they are deflected by considerations of immediacy of application, the more likely they are not only to contribute to human welfare, but to the equally important satisfaction of intellectual interest which may indeed be said to have become the ruling passion of intellectual life in modern times."

What is true of Heinrich Hertz working quietly and unnoticed in a corner of Helmholtz's laboratory in the later years of the nineteenth century may be said of scientists the world over for several centuries past. We live in a world that would be helpless without electricity. Called upon to mention a discovery or invention of the most immediate and far-reaching practical use we might well agree upon electricity. But who made the fundamental discoveries out of which the entire electrical development of more than one hundred years has come?

The answer is interesting. Michael Faraday's father was a blacksmith; Michael himself was apprenticed to a book-binder. In 1812—when he was already twenty-one years of age—a friend took him to the Royal Institution where he heard Sir Humphrey Davy deliver four lectures on chemical subjects. He kept notes and sent a copy of them to Davy. The very next year—1813—he became an assistant in Davy's laboratory, working on chemical problems. Two years later he accompanied Davy on a trip to the continent. In 1825, when he was thirty-four years of age, he became Director of the Laboratory of the Royal Institution, where he spent fifty-four years of his life.

Faraday's interest soon shifted from chemistry to electricity and magnetism, to which he devoted the rest of his active life. Important but puzzling work in this field had been previously accomplished by Oersted, Ampère, and Wollaston. Faraday cleared away the difficulties which they had left unsolved and by 1841 had succeeded in the induction of the electric current. Four years later, a second, equally brilliant, epoch in his career opened when he discovered the effect of magnetism on polarized light. His earlier discoveries have led to the infinite number of practical applications by means of which electricity has lightened the burdens and increased the opportunities and resources of modern life.

His later discoveries have thus far been less prolific of practical results. What difference did this make to Faraday? Not the least. At no period of his extraordinary career was he interested in utility. He was absorbed in disentangling the riddles of the universe—at first, chemical riddles, in later periods,

physical riddles. As far as he cared, the question of utility was never raised. Any suspicion of utility would have restricted his restless curiosity. In the end, utility resulted, but it was never a criterion to which his ceaseless experimentation could be subjected.

Let us look in another direction. In the domain of medicine and public health the science of bacteriology has played for half a century the leading rôle. What is its story? Following the Franco-Prussian War of 1870 the German Government founded a great university at Strasbourg. Its first professor of anatomy was Wilhelm von Waldeyer, subsequently professor of anatomy in Berlin. In his "Reminiscences" Waldeyer relates that among the students who went with him to Strasbourg during his first semester, there was a small, inconspicuous, self-contained youngster of seventeen, by name of Paul Ehrlich. The usual course consisted of dissection and microscopic examination of tissues. Ehrlich paid little or no attention to dissection, but, as Waldeyer remarks in his "Reminiscences":

"I noticed quite early that Ehrlich would work long hours at his desk, completely absorbed in microscopic observation. Moreover, his desk gradually became covered with colored spots of every description. As I saw him sitting at work one day, I went up to him and asked what he was doing with all his rainbow array of colors on his table. Thereupon this young student, in his first semester, supposedly pursuing the regular course in anatomy, looked up at me and blandly remarked, 'Ich probiere.' This might be freely translated, 'I am trying' or 'I am just fooling.' I replied to him, 'Very well. Go on with your fooling.' Soon I saw that without any teaching or direction whatsoever on my part I possessed in Ehrlich a student of unusual quality."

Waldeyer wisely left him alone. Ehrlich made his way precariously through the medical curriculum and ultimately procured his degree mainly because it was obvious to his teachers that he had no intention of ever putting his medical degree to practical use. He went subsequently to Breslau where he worked under Professor Cohnheim, the teacher of our own Dr. Welch, founder and maker of the Johns Hopkins Medical School. I do not suppose that the idea of use ever crossed Ehrlich's mind. He was interested. He was curious. He kept on "fooling." Of course his "fooling" was guided by a deep instinct—but it was a purely scientific, not a utilitarian motivation. What resulted? Koch and his associates established a new science—the science of bacteriology. Ehrlich's experiments were now applied by a fellow student, Weigert, to staining bacteria and thereby assisting in their differentiation. Ehrlich himself developed the staining of the blood film with the dyes on which our modern knowledge of the morphology of the blood corpuscles, red and white, is based. Not a day passes but that in thousands of hospitals the world over Ehrlich's technique is employed in the examination of the blood. Thus the apparently aimless fooling in Waldeyer's dissecting room in Strasbourg has become—without anyone's suspecting the result—a main factor in the daily practice of medicine.

I am not for a moment suggesting that everything that goes on in laboratories will ultimately turn to some unexpected practical use or that an ultimate practical use is its actual justification. Much more am I pleading for the abolition

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of the word "use" and for the freeing of the human spirit. To be sure, we will thus free some harmless cranks. To be sure, we will thus waste some precious dollars, but what is infinitely more important is the fact that we will be striking the shackles off the human mind and setting it free for the adventures which in our own day have taken Hale and Rutherford and Einstein and their peers millions upon millions of miles into the uttermost realms of space and loosed the boundless energy imprisoned in the atom. What Rutherford and others like Bohr and Millikan have done out of sheer curiosity in the effort to understand the construction of the atom has released forces which may transform human life, but this ultimate and unforeseen and unpredictable practical result is not offered as a plea in justification of their careers. Let them alone. No educational administrator can possibly direct the channels in which these or other gifted men shall work. The waste, I admit again, looks prodigious. It is not really so. All the waste that could be summed up in developing the science of bacteriology is as nothing compared to the advantages which have accured from the discoveries of Pasteur, Koch, Ehrlich, Theobald Smith, and scores of others—advantages that could never have accrued if the idea of possible use had governed their minds. These great artists—scientists and bacteriologists—disseminated the spirit which prevailed in laboratories in which for all they and others knew they were simply following the line of their own natural curiosity.

In this connection and in the atmosphere which envelopes the world today it is perhaps timely to emphasize the fact that the part played by science in making war more destructive and more horrible was an unconscious and unintended by-product of scientific activity. Lord Rayleigh, president of the British Association for the Advancement of Science, in a recent address points out concretely how the folly and stupidity of man, not the intention of the scientist, is responsible for the destructive use of the agents employed in modern warfare. The innocent study of the chemistry of carbon compounds, which has led to infinite beneficial results, incidentally showed that the action of nitric acid on substances like benzene, glycerine, cellulose, etc., resulted not only in the beneficent aniline dye industry but in the creation of nitroglycerin, which has uses good and bad. Somewhat later Alfred Nobel, turning to the same subject, showed that by mixing nitroglycerin with other substances, solid explosives which could be safely handled could be produced—among others, dynamite. It is to dynamite that we owe our progress in mining, in the making of such railroad tunnels as those which now pierce the Alps and other mountain ranges; but of course dynamite has been abused by politicians and soldiers.

Scientists are, however, no more to blame than they are to blame for an earthquake or a flood. The same thing can be said of poison gas. Pliny was killed by breathing sulphur dioxide in the eruption of Vesuvius almost two thousand years ago. Chlorine was not isolated by scientists for warlike purposes, and the same is true of mustard gas and dynamite. These substances could be limited to beneficient use, but when the aeroplane was perfected, men whose hearts were poisoned and whose brains were addled perceived that the aeroplane, an innocent invention, the result of long, disinterested and scientific effort, could

be made an instrument of destruction, of which no one had ever dreamed and at which no one had ever deliberately aimed.

What then must be the spirit and policy determining the course of the new Squibb Institute? The answer is easy: the fearless and unhampered search for truth, the unlimited cultivation of the natural curiosity of human beings within the field of science. It is almost certain that efforts aiming at the immediately practical will fail unless they are based upon a long succession of experiments and endeavors that have no such practical use in mind.

Unquestionably, disinterested scientists have accumulated knowledge which can and should be brought together for the purpose of relieving suffering, as happened, for example, in the case of insulin.

The history of science for two thousand years proves conclusively that no one can foretell or predict or plan the outcome of the untrammeled roving of the human spirit, searching for truth and truth alone. Whether these practical results shall be good or ill is no concern of those who have founded this institute. That is something that depends upon civilization. Civilized men will resolutely refuse the ill and embrace the good and, unless the world can be governed by the ideals of civilization, nothing can save it from ultimate destruction. If the destination of these resources is to be determined by the spirit and ideals of the men who have founded this institute and the men who are enlisted in it, then we can look forward to a world in which peace and beauty and health and all the other good things of the human spirit may determine the conduct and the character of our lives.

Let us therefore continue our quest for the useless as well as the useful, confident that in the long run both will inure to the benefit of humanity, as they have already done in the instances which I have given earlier in this address.

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Original Communications

THE USE OF PREDNISONE (METICORTEN) IN RESPIRATORY DISEASE

II. Pulmonary Emphysema and Pulmonary Fibrosis

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IN THE previous paper the results of the administration of prednisone ($A^{1,4}$-pregnadiene-17α, 21-diol-3, 11, 20-trione), Meticorten, to patients with bronchial asthma were reported.[1] This communication describes the effects of the drug in pulmonary emphysema and pulmonary fibrosis. Patients with chronic pulmonary disease in whom latent or overt failure of the right or left heart is present are often made worse when an increased burden is placed on the circulation by the accumulation of fluid that often accompanies the administration of cortisone, hydrocortisone, or ACTH. The favorable respiratory response of patients with pulmonary emphysema and pulmonary fibrosis to prednisone was especially advantageous since it was unassociated with salt and water retention in the therapeutic dosage used. This deleterious side effect had limited the usefulness of ACTH and cortisone in these disorders.

METHODS

The methods of administration of prednisone were in general similar to that described previously.[1] The drug was given in 4 divided doses, at mealtime and between 11 and 12 P.M., generally with milk or other fluid. In determining the most suitable dosage of prednisone for patients with pulmonary emphysema and pulmonary fibrosis, severe bronchospasm was considered an indication for dosages of 60 to 80 mg. per day for the first day or two, followed by a decrease

The prednisone used in this study was supplied by the Schering Corporation, Bloomfield, N. J. under the trade name of Meticorten.

of 10 to 20 mg. each two or three days thereafter depending upon the response of the patient. At the end of seven to ten days an approximate maintenance dosage of 10 to 25 mg. per day was adopted empirically.

In patients with a moderate amount of bronchospasm, in whom either maintenance therapy with hydrocortisone had been established or in patients in whom steroid treatment had not previously been used, 40 to 50 mg. of prednisone per day was administered at the start of the treatment; this was lowered at three-day intervals by 10 to 15 mg. per day to determine the minimal effective dose. Patients without evidence of heart failure were permitted an unrestricted diet, including as much salt as desired. In those cases in which salt restriction was indicated because of cardiac insufficiency, the restricted diet was maintained.

A total of 50 patients was studied. Twelve of these had extensive pulmonary fibrosis complicated by varying degrees of bronchopulmonary infections ranging from chronic bronchitis to bronchiectasis. Of the remaining 38 patients with pulmonary emphysema, 7 had an associated fibrosis as well. The response to treatment with either corticosteroids or ACTH had been documented in 18 of the 50 patients in this series.[2] The age, sex distribution, and dosage schedule of prednisone is illustrated in Table I.

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TABLE I. AGE, SEX DISTRIBUTION, AND AVERAGE DOSAGE OF PREDNISONE IN 50 PATIENTS WITH PULMONARY EMPHYSEMA AND FIBROSIS

AGE (YEARS)		SEX		AVERAGE DAILY DOSE (MG.)			
				INITIAL		MAINTENANCE	
MEAN	RANGE	MALE	FEMALE	1ST DAY	1ST WEEK	DAILY	NUMBER OF DAYS
58.0	15–74	39	11	50	35	20	60.0

Ventilatory function studies were performed on the hospitalized and selected office patients and included the maximal vital capacity recorded after a full inspiration and a gradual nonforceful expiration, the resting minute ventilation breathing air and 100 per cent oxygen, and the maximal breathing capacity. These measurements were obtained with a closed circuit Benedict-Roth spirometer and the data evaluated with respect to previously published observations.[1-4]

Daily body weights and blood pressures were recorded in the hospitalized patients and once or twice weekly in the ambulatory cases. Serum sodium, potassium and chlorides, blood pH, and 24-hour urinary 17-ketosteroids were followed in 2 patients who were maintained on a constant dietary regimen.

RESULTS

The bronchodilator response to prednisone of patients with chronic pulmonary emphysema was similar to that observed with the adrenocortical hormones used in the past, but certain other unique differences of a favorable nature were observed, especially in some of the cases of pulmonary fibrosis.

In the majority of all patients treated, clinical evaluation revealed that a prompt remission of dyspnea took place; a more rapid response was especially evident in those cases previously treated with cortisone or ACTH. The mean onset of subjective improvement, as determined by a diminution in dyspnea, and wheezing, occurred forty-four hours after the start of therapy. Thirty-two per cent of the patients noted some relief within twenty-four hours, while 8 per cent required an excess of seventy-two hours of drug administration before noticing any improvement. This is illustrated graphically in Fig. 1. Fifty-eight

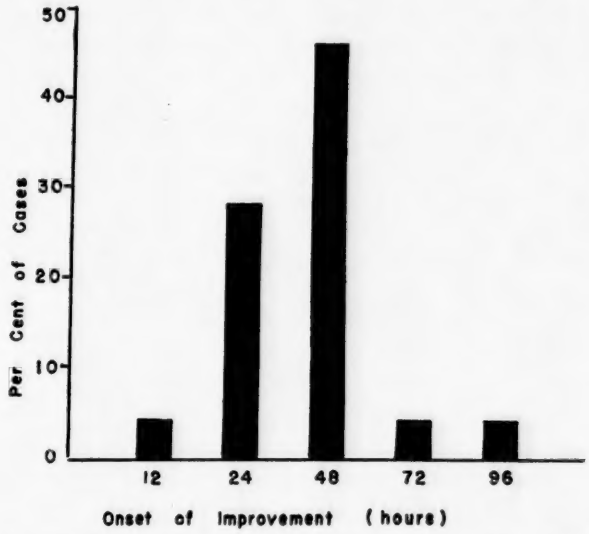

Fig. 1.—Fifty patients with pulmonary emphysema. The time-relationship of the onset of subjective improvement of dyspnea occurred in the majority of patients within forty-eight hours after the start of prednisone therapy.

per cent (29 of the 50 patients) showed marked improvement, evidenced by cessation of wheezing, relief of dyspnea, and conspicuous increase in exercise tolerance. Fourteen obtained moderate benefit and 7 patients had little or no relief with prednisone. This is presented in Table II.

TABLE II. CLINICAL IMPROVEMENT RESULTING FROM THE USE OF PREDNISONE IN PULMONARY EMPHYSEMA AND FIBROSIS

NUMBER OF CASES	MEAN ONSET OF IMPROVEMENT (HOURS)	CLINICAL IMPROVEMENT*		
		MARKED	MODERATE	NONE
50	44	29	14	7

*Marked — Relief of dyspnea and wheezing with increase in exercise tolerance.
Moderate — Partial improvement of dyspnea and lessening of bronchospasm requiring supplementary medication.

The vital capacity was obtained on 15 patients before and during prednisone therapy. The mean increase was 32 per cent. In Fig. 2, a graphic plot of the individual data is expressed as per cent of the predicted normal capacity using the regression formula of Baldwin, Cournand, and Richards.[4] It is of interest that 2 of the first 5 subjects who showed no significant change had extensive pulmonary fibrosis; and the remaining 3, with severe emphysema, had little or no bronchospasm. In the 6 patients exhibiting the most marked increases in vital capacity, clinical evidence of bronchospasm was a prominent feature. Subjects 6, 7, and 8, who showed an intermediary response, were being maintained on hydrocortisone prior to this study. The spirographic tracing of a patient with pulmonary emphysema and pulmonary fibrosis showing a 75 per cent increase in vital capacity is presented in Fig. 3.

A mean increase of 21 per cent in the maximal breathing capacity was recorded during the administration of prednisone. In Fig. 4 a graphic tracing of a patient with severe pulmonary emphysema reveals an increase in maximal breathing capacity from 16 to 21 L. per minute.

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Fig. 2.—Vital capacity of 15 patients with pulmonary emphysema. The more striking increases in vital capacity after prednisone occurred in those patients who exhibited clinical evidence of bronchospasm and had not been previously maintained on cortisone.

The mean resting minute ventilation before therapy was 11.3 L. per minute breathing air, and 6.9 L. per minute when 100 per cent oxygen was inhaled. While the patients were on prednisone, this ventilatory difference between air and oxygen became negligible: 8.8 L. per minute for air and 8.2 L. per minute for oxygen.

In contrast to previously observed effects of the corticosteroids, 12 of the 50 patients had a weight loss ranging between 3 to 9 pounds associated with the administration of prednisone, while the remainder maintained their initial weights. Five of these 12 patients with pulmonary emphysema (4 with cor pulmonale) were being maintained on hydrocortisone at the time prednisone

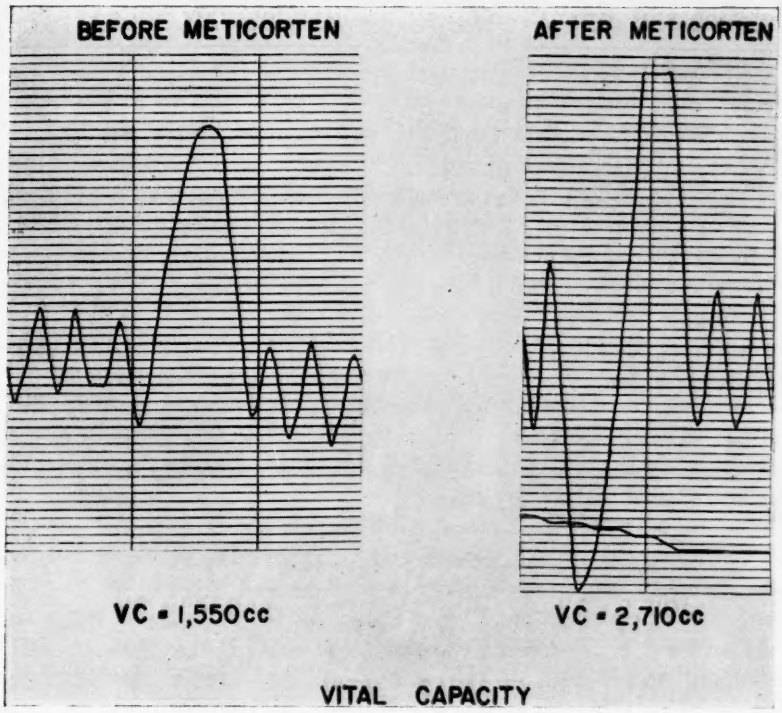

Fig. 3.—Increase in vital capacity with Meticorten therapy in patient with pulmonary emphysema and fibrosis. A 75 per cent increase in vital capacity was observed during prednisone (Meticorten) therapy. It is of interest that this gain occurred for the most part in the expiratory reserve volume.

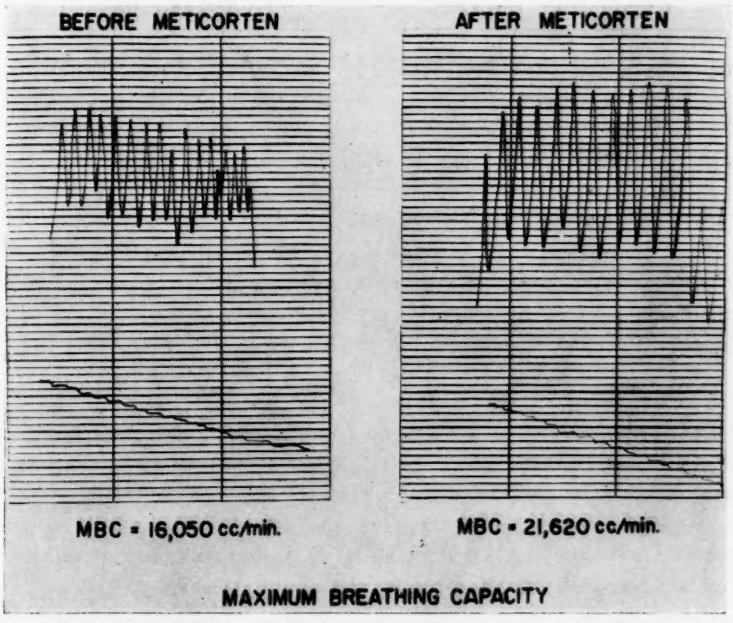

Fig. 4.—Increase in maximum breathing capacity with Meticorten therapy in patient with pulmonary emphysema and fibrosis. A significant increase of 34 per cent in the maximum breathing capacity is observed in a patient with severe ventilatory insufficiency.

was substituted. An additional 3 patients in this category who had not previously received steroid therapy, and who were in overt or borderline right heart failure, lost an average of 4 pounds in the first week of prednisone treatment.

Of interest was the finding of a moderate to marked weight loss in 4 patients with pulmonary fibrosis in whom cardiac failure had not been demonstrated and in whom cortisone had not been employed, and in whom therefore previous accumulation of fluid could not be ascribed to this steroid. In the first 2 cases described in the histories which follow, a weight loss of 8 to 9 pounds, respectively, took place during the first week of prednisone study. In the other 2, including 1 case of silicosis, the weight loss was 4 pounds. In all of these instances food intake was, if anything, increased. A possible explanation for this response to prednisone will be discussed under Comment. The onset of improvement in this group accompanied by loss of weight was an apparent significant factor in relief of dyspnea.

The serum sodium, potassium, chlorides, carbon dioxide and pH in the 2 patients who were on a balance study throughout their course showed no significant changes. After two months of maintenance therapy on 15 to 20 mg. of prednisone daily, 1 patient had a reduction in the urinary 17-ketosteroids from 15.2 to 7.7 mg. Following cessation of therapy and the administration of 60 units of ACTH gel daily for ten days, the 17-ketosteroids rose to 13.9 mg.

Three patients who had been on long-term hydrocortisone maintenance therapy showed a diminution in facial fullness after two weeks of prednisone. Two patients with generalized psoriasis had marked improvement in the skin lesions with prompt relapse on cessation of therapy, and 1 patient with a severe corneal ulcer which had been resistant to previous therapy healed rapidly while on prednisone.

Adverse side effects included transitory headache in 2 patients, and increased nervous tension in 2 accompanied by paresthesia in 1 subject; reactivation of a latent bronchopulmonary infection in 3 patients, and gastrointestinal discomfort consisting of distention or epigastric pain in 6 patients. Thrombophlebitis of the lower extremity occurred during therapy in one patient and slight "moon face" was observed in 2 instances.

In order to indicate the incidence of side reactions, the total number of patients treated with prednisone have been reviewed. These included the 50 subjects in the present study, 30 patients with bronchial asthma previously reported, and an additional 40 patients; 18 with bronchial asthma and 22 with pulmonary emphysema, who were not included in these studies. Of these 120 patients, 27 per cent reported undue side effects which were for the most part mild and transitory in character, disappearing when the dosage of prednisone was reduced or discontinued. Of special interest, however, where the 10 patients who complained of gastrointestinal discomfort. One of these had a reactivation of a peptic ulcer with gastrointestinal bleeding after five days of prednisone therapy. Six patients had a flare-up of a latent sinobronchopulmonary infection which responded to appropriate antibiotic therapy.

The case histories of 5 patients who revealed a significant weight loss while receiving prednisone are reported.

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CASE 1.—Man, aged 69 years. Diagnosis: Pulmonary fibrosis, bronchiectasis, and pulmonary emphysema.

Increasing shortness of breath was noted during the previous four years during which time the patient had three attacks of pneumonia. Six months prior to admission, persistent coughing and shortness of breath on slight exertion became exceedingly troublesome. On examination, in November, 1954, the breathing was shallow and costal, with a rate of 34 per minute at rest, and the nail beds were cyanotic. Frequent paroxysms of coughing resulted in the occasional production of seromucoid expectoration. Laboratory examination of the sputum revealed a moderate number of pus cells which yielded colonies of *Staphylococcus aureus* and a nonhemolytic streptococcus on culture. X-ray of the lungs showed pulmonary fibrosis, slight in the right lung but marked throughout the left lung, with a shift of the mediastinum toward the left side. Thoracotomy and biopsy of the left lung revealed bronchiectasis and pulmonary fibrosis of nonspecific origin. With the use of breathing exercises including diaphragmatic respiration, and a course of antibiotic therapy including tetracycline and streptomycin, the patient manifested marked improvement with virtual elimination of cough and a lessened degree of dyspnea.

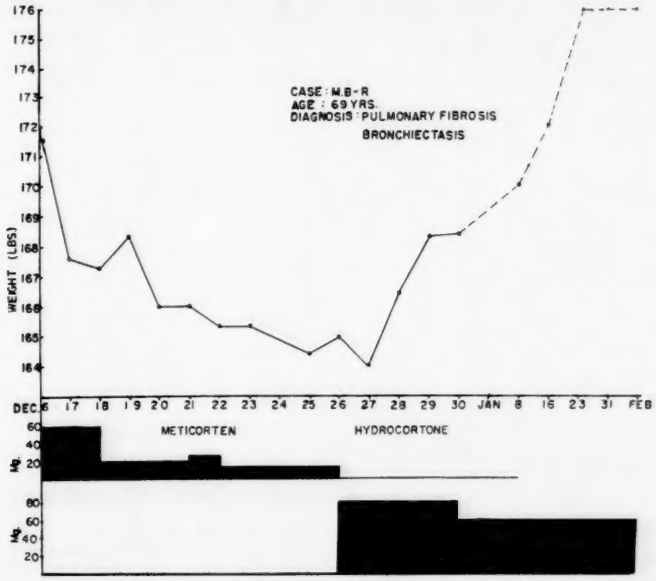

Fig. 5.—A weight loss of 8 pounds occurred during the first eleven days of prednisone (Meticorten) therapy. The substitution of hydrocortisone resulted in fluid retention with a prompt increase in weight exceeding the initial level.

The administration of 30 mg. of prednisone daily for one week was followed by further clinical improvement, especially in an increased capacity for exertion without dyspnea, and a subjective feeling that his chest was "lighter," the latter response noted during the first twenty-four hours of treatment. The arterial oxygen saturation of 91 per cent was not significantly altered at the end of one week's treatment; the CO_2 content of 44 volume per cent remained unchanged. However, a weight loss of 8 pounds took place during the first eleven days of treatment. The patient at this time was on a standard hospital diet with no additional salt. When hydrocortisone was substituted, 60 mg. per day for five days on the same diet, a weight gain of 4½ pounds resulted. This is illustrated in Fig. 5. Subsequently, when the patient returned to his home and hydro-

cortisone was continued at 60 mg. daily, a further weight gain of 7 pounds took place, despite the ingestion of Diamox, 250 mg. three times weekly, and Neohydrin, 2 tablets twice weekly, and a low sodium diet. Dyspnea, cough, and tenacious expectoration recurred despite continuation of antibiotic and bronchodilator therapy. Administration of prednisone was contemplated when the patient suddenly died in February, 1955, shortly after admission to a local hospital. In the opinion of the attending physician, the sudden collapse and death were due to cardiac failure. The autopsy revealed a severe degree of honeycombing of the left lung, extensive diffuse fibrosis in the right lung, hypertrophy, and dilatation of the right heart, evidence of bronchial infection and scattered areas of passive congestion and edema.

Although considerable clinical improvement had taken place during the month of hospitalization prior to drug administration, a further unmistakable increase in exercise tolerance and relief of dyspnea occurred while he was on prednisone. The loss of 8 pounds in body weight was surprising since there were no overt manifestations of cardiac insufficiency, i.e., venous pressure, electrocardiogram, and heart size by roentgenogram were normal. Nevertheless, latent congestive failure may have been present, since a rapid gain of 11 pounds occurred when hydrocortisone was substituted despite salt restriction and diuretics. The patient became progressively worse during hydrocortisone therapy, and although extensive pulmonary disease was present, it is impossible to dismiss the adverse effect of fluid retention as a significant factor in the terminal cardiac failure.

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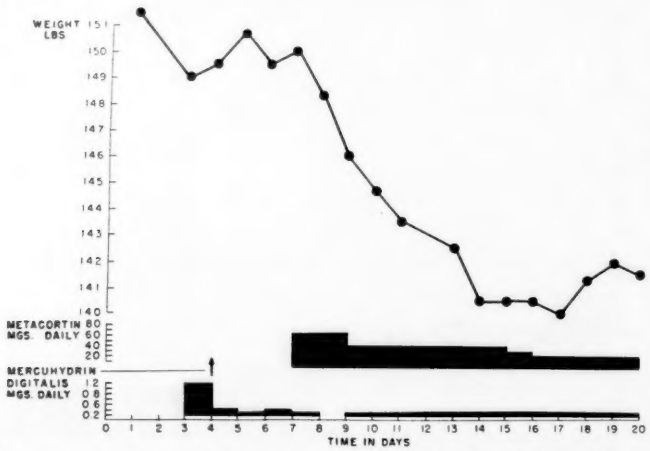

Fig. 6.—A graphic illustration of the weight loss accompanying prednisone (Meticorten) therapy in a patient with pulmonary fibrosis who had previously been unresponsive to digitalization and mercurial diuretics.

CASE 2.—Woman, aged 62 years. Diagnosis: Pulmonary fibrosis.

This patient with advanced pulmonary fibrosis was admitted to the hospital in January, 1955, because of increasing dyspnea of sixteen months' duration, accompanied by a chronic cough productive of mucoid sputum. She was markedly cyanotic and dyspneic on the slightest exertion. Many moist râles were present over both lungs posteriorly. Despite digitalization, mercurial diuretics, antibiotic therapy, and oxygen, dyspnea was not relieved and she lost only 1 pound from her initial weight of 152 pounds during the first six days of hospitalization. A course of prednisone consisting of 80 mg. daily for two days; 60 mg. daily for six days, and 40 mg. for one day, followed by a maintenance dose of 20 mg. daily resulted in marked relief of dyspnea and decrease in cyanosis within eighteen hours of initiation of therapy. Fig. 6 presents graphically

the weight loss of 10 pounds which occurred during the first week of prednisone therapy. X-rays of the chest taken on the fifth day of therapy revealed clearing in the mid-portion of the right lung and markedly improved aeration in the left lower lung field. This is illustrated in Fig. 7. The erythrocyte sedimentation rate, which had been 81 mm. per hour (Westergren) before the administration of prednisone, fell to 21 mm. per hour. Clinical improvement was maintained in the hospital by a daily dose of 15 mg. prednisone.

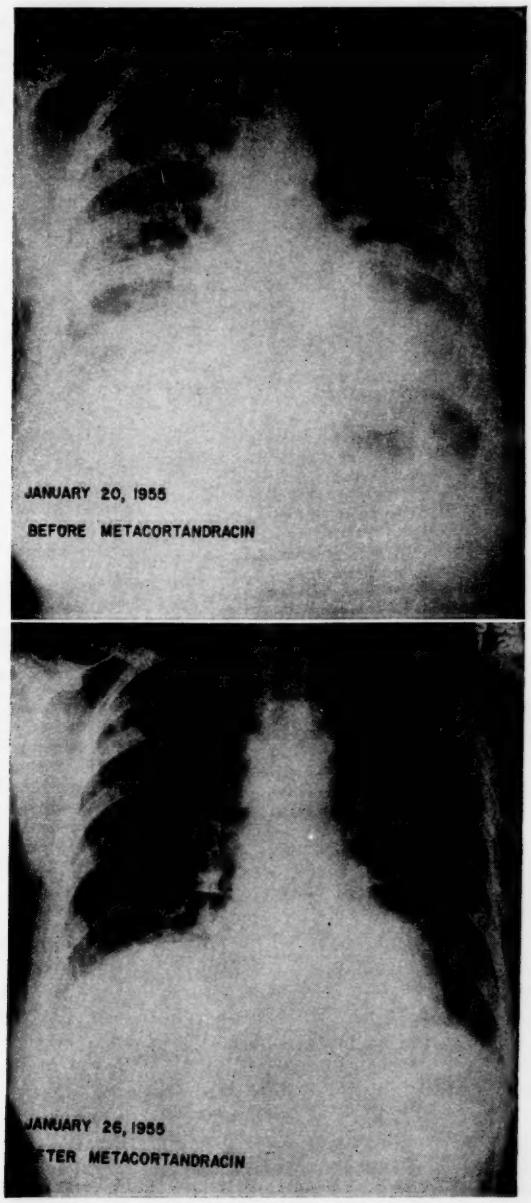

Fig. 7.—Chest roentgenograms revealing clearing of both lung fields after five days of prednisone (Meticorten) therapy.

CASE 3.—Man, aged 56 years. Diagnosis: Pulmonary emphysema and fibrosis and chronic lymphatic leukemia.

This patient with a seven-year history of chronic lymphatic leukemia was admitted to the hospital because of fever, chills, cough, chest pain, and increasing dyspnea of three days' duration. In 1953 he had had two episodes of pneumonia which were followed by increasing exertional dyspnea only partially relieved by nebulized 2.25 per cent racemic epinephrin (Vaponefrin). X-ray revealed marked hilar adenopathy and diffuse nodular shadows of increased density throughout both lung fields. Although the patient responded to penicillin and streptomycin with a decrease in temperature and cough, shortness of breath and bronchospasm persisted. A 17-day course of cortisone produced a weight rise of 7 pounds without relief of dyspnea. Prednisone, 60 mg. daily, was followed within forty-eight hours by clinical improvement, which became more marked following a diuresis with the loss of 8 pounds during the next seven days, as seen in Fig. 8. Ankle edema, which had occurred during the administration of cortisone, disappeared, and he was subsequently placed on a maintenance dose of 20 mg. of prednisone daily.

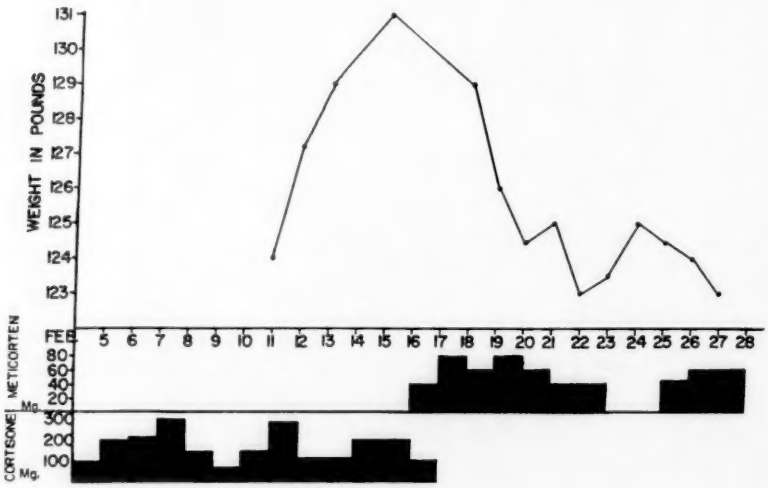

Fig. 8.—A comparison of the effect of cortisone and prednisone (Meticorten) on fluid retention as demonstrated by weight change in a patient with chronic lymphatic leukemia accompanied by pulmonary emphysema and fibrosis.

CASE 4.—Woman, aged 58 years. Diagnosis: Pulmonary emphysema and bronchial asthma.

Repeated attacks of bronchial asthma, loss of consciousness, and convulsive seizures had occurred since 1930. During the week prior to hospital admission, dyspnea increased in severity and was accompanied by cyanosis and disorientation which rapidly progressed to a semicomatose state. On admission, in January, 1955, the patient appeared critically ill with clinical signs of severe pulmonary insufficiency and right heart failure. Cyanosis was profound, and breath sounds were barely audible. The arterial oxygen saturation was 64 per cent; blood pH 7.23 with a P_{CO_2} of 100 mm. Hg. The patient was digitalized, given Mercuhydrin and placed on intermittent positive pressure breathing. Deepening coma and obstruction to the airway necessitated a tracheotomy following which she was placed in a tank respirator. The administration of

intravenous aminophylline, salicylates, and antibiotics had no significant effect on either her state of consciousness or respiratory failure. On the fourth day after admission she was started on prednisone, receiving 80 mg. over the first twenty-four hours, followed by 60 mg. daily for two days, 40 mg. for one day, and a maintenance dose of 20 mg. daily thereafter. Mechanically assisted respiration by the tank respirator was augmented by exsufflation with negative pressure for more adequate hyperventilation. Within thirty-six hours of the onset of prednisone and the therapeutic measures designed to increase pulmonary ventilation and bronchial drainage, striking improvement was observed. She regained consciousness, responded to questioning in a coherent manner and appeared to have less difficulty in maintaining spontaneous breathing. By the fifth day of therapy, she was removed from the respirator. At this time, the arterial oxygen saturation was 66.8 per cent; pH 7.40 and P_{CO_2} 70 mm. Hg. Progressive improvement resulted in her discharge from the hospital on a daily dose of 20 mg. of prednisone which was found essential for the maintenance of her remission. Improvement has been maintained on this dosage during a five month follow-up in the outpatient clinic. During this period she has been able to return to work.

CASE 5.—Man, aged 65 years. Diagnosis: Pulmonary emphysema and cor pulmonale.

Repeated episodes of respiratory infections diagnosed as pneumonia preceded the onset of progressive dyspnea seven years before. Chest films revealed the characteristic picture of advanced pulmonary emphysema. Temporary improvement occurred when cortisone was administered two years before, but resulted in salt and water retention manifested by pretibial edema. Moderate benefit was obtained from the use of bronchodilator aerosols, and training in viscerodiaphragmatic breathing. Because of increasing right heart failure, the patient was digitalized and placed on a low salt diet with the addition of Diamox, 250 mg. daily. Prednisone, 30 mg. daily, was administered for the first five days with marked relief in dyspnea, noted after twenty-four hours. On a maintenance dose of 25 mg. daily, improvement continued and a loss of 6 pounds in body weight occurred during the first five weeks. He had been on maintenance therapy for the past five months. Lowering of the dose to 15 mg. daily resulted in the return of dyspnea and the minimal dosage for adequate maintenance appeared to be 20 mg. daily. Except for an episode of thrombophlebitis of the left leg from which he recovered in two weeks without sequelae, the patient has felt better than at any time in the previous three years.

COMMENT

The symptomatic benefit which followed the administration of prednisone was impressive in this series of patients with pulmonary emphysema and pulmonary fibrosis. Relief of dyspnea and increase in exercise tolerance occurred with dosages one-fourth to one-fifth the amount employed with cortisone or hydrocortisone. The maintenance level was similarly reduced. In addition, supplementation with potassium chloride and the strict adherence to a low sodium diet was not required except for those patients in heart failure who had been on a low salt regimen prior to therapy. The psychological benefit of an unrestricted diet during long-term therapy contributes in no small way to the general sense of well-being.

The variable response to ACTH and cortisone in this group of patients with combined ventilatory and alveolar-capillary dysfunction has been previously described.[5-7] The improvement in ventilatory function produced by prednisone

probably resulted in part from a reduction in mucosal edema, inflammatory or allergic, of the tracheobronchial airway as well as relief of bronchospastic dyspnea. In addition, an improved oxygen diffusion seemed to take place in those patients with pulmonary fibrosis in whom little or no bronchospasm was detected clinically. This is indirectly substantiated by the decrease in the resting minute ventilation during prednisone therapy and more especially by the reduction in the air-oxygen ventilatory difference when 100 per cent oxygen was substituted for room air.

The loss of weight in 4 patients with pulmonary fibrosis was particularly striking and deserves further study. In the absence of overt cardiac failure, it is interesting to speculate that some of the fluid lost may have come from inflammatory or granulomatous tissue in the lung. Prednisone also produced a diuresis and weight loss in five patients who had clinical evidence of fluid retention while on maintenance cortisone therapy and in three with cardiac insufficiency who had not previously had treatment with cortisone.

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Among the factors responsible for the diuresis encountered may be included relief of hypoxia with or without cardiac insufficiency. Hypoxia, which may increase capillary permeability, may have been decreased by prednisone as a result of a diminution in obstructive dyspnea through its anti-inflammatory activity and the decrease in bronchospasm. Improved ventilation of the lungs with an increased tissue oxygen tension may therefore have resulted in a diuresis which in many respects is similar to that produced by oxygen inhalation in chronic cardiorespiratory disease.[8] Two patients with pulmonary fibrosis of unknown etiology, not included in this series, have recently been treated with prednisone and although both were clinically improved, no diuresis or weight change occurred. Neither of these patients was cyanotic, and it is possible that in the absence of hypoxia, diuresis does not take place.

Although the longest period of observation in patients on maintenance therapy is only five months, several adverse reactions previously described with cortisone and ACTH have been encountered with prednisone, with the exception of salt and water retention.[9,10] Of importance was the occurrence in 6 cases of reactivated sinobronchopulmonary infection and the relatively high incidence of epigastric pain or flatulence after eating. As a precautionary measure, prednisone is administered with milk and the addition of aluminum hydroxide or calcium carbonate two hours after meals and on retiring. Bollet, Black, and Bunim[11] have also recently advocated the routine coadministration of an aluminum hydroxide gel as a precautionary measure. The neutralization of gastric acidity by adequate antacid therapy facilitates the healing of peptic ulcer and may prevent serious complication.[12] Concurrent administration of the broad spectrum antibiotics such as tetracycline was often employed in patients with bronchitis or bronchiectasis.

SUMMARY

The effect of prednisone was studied in 50 patients with pulmonary emphysema and pulmonary fibrosis. The clinical results differ from those obtained with cortisone and ACTH in the following ways:

1. Moderate to excellent improvement with relief of dyspnea and increased exercise tolerance in 86 per cent of the patients treated with a daily dosage averaging one-quarter that employed with cortisone.

2. The onset of subjective improvement was significantly more rapid than cortisone, usually within forty-eight hours of initiation of therapy.

3. A striking weight loss ranging between 3 to 9 pounds occurred in 12 of the 50 patients during the first week of therapy including cases of cor pulmonale who had not responded favorably to cortisone. Of interest was the finding of loss in body weight in 4 patients with pulmonary fibrosis who had not previously been treated with cortisone. There was a decrease of 8 and 9 pounds, respectively, in 2 of these patients during the first week of treatment. The possible mechanism of this weight loss at a time when appetite and food intake was increased deserves further study.

4. With the exception of salt and water retention, and the decreased incidence of facial mooning or fat deposition, other adverse reactions observed with cortisone have been encountered, especially gastrointestinal disturbances and reactivation of sinobronchial infection. Appropriate measures to counteract or prevent these conditions have been suggested.

The case histories of 5 patients who exhibited significant weight loss are reported.

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HOSPITAL CARE OF ORTHOPEDICALLY HANDICAPPED CHILDREN IN NEW YORK CITY

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DURING the last three years the Bureau for Handicapped Children of the Department of Health has developed a Hospital Consultation Program for the survey of orthopedic services throughout New York City. It represents the first such plan established in this country by a public health agency, and is but one of a group of pilot studies and programs of the Bureau. We hope that it will not only accomplish its stated purpose of improving care, but will stimulate responsible public health agencies of other communities to do the same. It might also serve as the foundation for methods which could be utilized in other Crippled Children's Programs.

Financially, New York City and New York State share equally in the payment for children under the age of 21 who have orthopedic disabilities requiring hospital, convalescent, or rehabilitation care, as well as for their braces and appliances. Until recently, little attention was paid by the Department of Health to the quality of care given or the facilities and caliber of the institutions in which this care was rendered. About three years ago it became keenly felt that the responsibility for distribution of monies for orthopedic care carried with it a concomitant responsibility to be sure that the care given was the best that modern orthopedic surgery could offer. As a result, the Orthopedic Advisory Committee of the Bureau for Handicapped Children, under the chairmanship of Dr. Philip Wilson, along with the Bureau personnel, formulated a set of standards that was felt to represent a definition of good care for orthopedically handicapped children.

With these standards as a guide, hospitals and convalescent institutions participating in the State Aid Medical Rehabilitation Program, as well as those desirous of becoming part of the Program, are surveyed by a team from the Bureau for Handicapped Children. This team consists of the Bureau Director, who is a pediatrician, the Senior Orthopedic Consultant, and Consultants in Physical Medicine and Rehabilitation, Pediatrics, Nursing and Social Service.

Presented at the Orthopedic Section, New York Academy of Medicine, Feb. 19, 1954.

The team meets with the directors and representatives of these various hospital services as a group to review the orthopedic and related facilities. The survey consists of a preliminary discussion of these facilities followed by case rounds with the attending staff on all orthopedic patients under the age of 21. All services, including pediatric, physical and occupational therapy, operating room, x-ray and laboratory are also visited, and the charts and records reviewed. Usually a second visit is required to survey the Orthopedic Out-Patient Department.

The findings of the survey are presented at a periodic meeting of the Orthopedic Advisory Committee. The committee consists of 21 community leaders in the fields of Orthopedic Surgery, Pediatrics, Physical Medicine and Rehabilitation, Social Service, Nursing, Vocational Rehabilitation, and Hospital Administration. After thorough consideration of the report, the Advisory Committee suggests approval or disapproval of the institution with recommendations as to means whereby the services can be improved. This decision, as well as the list of recommendations, are discussed at a subsequent conference at the hospital, the Bureau offering its assistance in any means possible. Conditional approval is occasionally suggested, and disapproved institutions may reapply for participation in the Program when they feel they have made headway in developing their services. Periodic resurvey of all institutions is an integral part of the Program.

Most institutions with organized orthopedic services are desirous of participating in the State Aid Program for two principal reasons: first, to receive payment for the care of orthopedically handicapped children treated at the hospital; and, second, to expand their orthopedic services by referrals from the various agencies throughout the city which are more likely to send patients to an approved institution where payment for care and appliances is assured.

The material presented represents a survey of 24 hospitals in New York City which participate, or have requested participation, in the Orthopedic Program.

The set of standards established by the Orthopedic Advisory Committee and the Bureau for Handicapped Children is used as the basis of consideration for approval of the services surveyed, and for the recommendations made after the survey. It must be admitted that the standards represent ideal orthopedic and related care, and few institutions meet all of the requirements at present. A hospital, therefore, is usually approved if it *reasonably* meets the essential standards, provided that good general care is offered, and that the hospital is interested and anxious to improve its services. It is considered essential that the hospital have the approval of the Joint Commission on Accreditation, and the American Medical Association Council on Medical Education for training of Residents in Orthopedic Surgery and Pediatrics.

Only 8 of the 24 hospitals had full three-year approval for resident training in orthopedics, 4 had two-year approval, 3 had one-year approval, and 9 had no approval; this indicates that only one-third of the hospitals had full residency approval, and over one-third had no approval at all. Yet orthopedic patients were being seen regularly and cared for in all of these institutions.

In 17 of the 24 hospitals the orthopedic service was a separate department. In 3 hospitals it was part of the general surgical service, and in 4 there was no service at all. In 21 of the 24 services, the Chief was a qualified orthopedic surgeon, but only 15 of the 24 (or 62 per cent) had solely orthopedists on the staff. Three hospitals had qualified orthopedists on a consultant basis only. In only half of the hospitals was there a separate orthopedic house staff.

In almost all instances routine attending orthopedic rounds were made at least once a week, with 13 institutions having daily attending rounds. Usually grand rounds were considered as a function of the orthopedic service alone, and were made only by the orthopedists and the nurses assigned to the particular wards. In 5 institutions social service workers accompanied the orthopedists and in only 3 did the pediatrician come on children's orthopedic rounds. In only 5 was the Department of Physical Medicine and Rehabilitation represented. In staff conferences as well, orthopedists usually attended alone. It was the distinct impression that much better over-all and coordinated care was given when rounds and conferences represented a team effort on the part of all of the related services. Too often social service, pediatric, nursing, or physical therapy problems may be overlooked and never properly followed through, unless representatives of these services are there when the child is presented and discussed.

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A qualified pediatric staff is considered an essential factor in the care of orthopedically handicapped children. In 22 of the 24 institutions there was a qualified Chief of Pediatrics, and 17 or 70 per cent had some degree of approval for training of pediatric residents. It is surprising that with such relatively adequate facilities for pediatric care in most of the hospitals seen, there is generally poor liaison between the pediatrician and the orthopedist. In only 6 institutions did the pediatrician see the orthopedic children routinely on admission, and in still fewer did they follow the children during their hospital course. In others, pediatricians saw patients only on consultation. This relatively poor liaison has been emphasized in recommendations and at hospital conferences, using our own survey team as an example of how pediatrician and orthopedist can assist each other in the care of handicapped children. Although there is a universal desire to improve care along lines of better liaison between services, these conferences frequently seemed to be the first time both the hospital pediatrician and orthopedist have met to review possible means of cooperation. An important first step, therefore, is to bring the proper personnel together to discuss it, demonstrate its practicality, and offer suggestions based on experiences of other institutions as so how they have overcome their obstacles and problems

The standards call for a Department of Physical Medicine and Rehabilitation under a qualified director. There were 8 approved residencies in the 24 hospitals surveyed, and most departments were poorly developed. There were 13 qualified active chiefs of service, and in 4 institutions there were qualified chiefs on paper only, who did not actively participate in the rehabilitation programs. Only about half of the institutions surveyed had separate departments of physical medicine. Because of generally poor liaison between orthopedics and physical medicine, and frequently inadequate over-all medical supervision, there was

almost a universal overuse of physical therapy. The nature of physical therapy given in a high proportion of institutions represented application of heat in various forms, and use of expensive impressive machines, with seemingly little understanding as to the basic concepts of rehabilitation itself.

In 7 institutions, consultations in the various other medical specialty services were not too readily available. There was 100 per cent social service coverage of orthopedically handicapped children in only one-third of the hospitals surveyed.

It was generally noted that the hospitals underuse convalescent facilities, and keep patients in their own hospitals for extended periods of time. This accounted for the relatively high census of some children's orthopedic services, in the light of a low surgical load. In one instance a large service was not familiar with convalescent facilities in the city, and such cases as Perthes' disease were kept in the hospital for a year or more.

There was also generally poor use of public health nurse, or visiting nurse services, particularly for interval care where children in plaster casts, or those requiring prolonged bed rest, with a minimum of medical supervision, can be cared for adequately at home.

In reference to the large amount of overinstitutionalization in hospitals and convalescent homes, our experiences in another new approach to the problems of the orthopedically handicapped child should be mentioned. A Review Committee has been established, meeting weekly and reviewing all cases that have had 6 months or more of institutionalization,* either consecutively or intermittently, where requests have been made for further inpatient care. Of 210 children reviewed during the first six-month period, recommendations were made that 48 (approximately one-fourth) of the children should bedisch arged, with or without recommendations as to social service assistance. Forty-seven of these 48 were discharged during that period, indicating that not only were one-fourth of the patients overinstitutionalized, but that, with social service assistance in many cases, discharges could be arranged. Of the 59 cerebral palsy children reviewed, it was recommended that 25, or almost half, be screened for a cerebral palsy school unit. Many of the cerebral palsy children had never been tested psychologically for educability, and huge sums of money had been spent in years of expensive inpatient care on several children, who, on evaluation, were of imbecile level, and should have been at home or in custodial institutions.

The entire approach has been toward reducing overinstitutionalization and returning children to as normal a home life as possible without jeopardizing good medical care. Although in a few cases overinstitutionalization appeared to be a conscious effort to boost census, it usually reflected the unfamiliarity of the staffs with facilities available in the community to cope with the problems

*After the first six months of operation of the Review Committee, it has been so successful that the period of institutionalization before review has been reduced to ninety days. All cerebral palsy cases in the school age group are screened for the cerebral palsy school units before any inpatient nonsurgical care is approved. Home conditions are carefully investigated before any cases are approved for convalescent care that might be conducted at home with Visiting Nurse Service assistance. To date, about 500 cases have been reviewed.

of the handicapped child. Incomplete or inadequate continuous medical supervision, and poor teamwork between the orthopedic and related services, particularly social service, may result in the "forgotten child," who just stays on and on.

In the light of a far greater number of beds available for the care of orthopedically handicapped children in the city, as compared to the relatively smaller number of children requiring this attention, what should be the attitude of the public health agency which pays for this care? Should approval be limited to only those institutions affording the finest care within the limits of the needs of the community, and efforts and finances devoted to still further improvement of these facilities? Or should approval be given to a large number of institutions, each with small orthopedic services and insufficient case material for resident training? We are unable to answer this question at present, and depend upon the advice and help of the Orthopedic Advisory Committee and the practicing orthopedists and pediatricians in the city for guidance. It is hoped that the problem will solve itself through a process of "natural selection," where institutions offering good care, which are anxious to grow, will continue as the core of the Handicapped Children's Program, and those who cannot or, in reality, do not care to develop outstanding departments may want to drop out of the Program.

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Following the Hospital Survey, a revisit is made to the Orthopedic Out-Patient Department. Three institutions treating handicapped children had no orthopedic clinic. In only one-third of the hospitals was a children's orthopedic clinic a separate division of the outpatient department. A pediatrician was in attendance at the Orthopedic Clinic in only *two* instances. It was surprising to note the relatively small effort made to develop good outpatient facilities for the handicapped child, compared to the relatively greater efforts directed toward the development of inpatient services. In most instances it was felt that regular attendance at the children's orthopedic clinic by a pediatric resident would serve the purpose of team supervision of orthopedic-pediatric problems as well as pediatric resident training in orthopedics. Although pediatric residencies often include orthopedic lectures and care of hospital cases, only in the outpatient department does the pediatric resident come into contact with the type of ambulatory problems that he is most likely to meet in his daily practice, and obtain training in the early recognition of conditions requiring prompt orthopedic treatment. The need for strengthening outpatient departments will become more pressing as overinstitutionalization is reduced, and more patients are treated at home. In all instances where separate children's orthopedic clinics have been developed, it was the general feeling that they were worth while from the point of view of better patient care and better staff teaching. In several overcrowded clinics the diagnostic facilities were poorly used, and institutions were prone to admit children for examinations that could have been done in the clinic. A large number of clinics are seriously understaffed, with more than half having an inadequate number of staff members in attendance. Two clinics had as few as one physician attending to 80 to 100 patients. None of the clinics had time-appointment systems, which means long periods of wait-

ing for children, infants, and mothers on clinic benches. Physical facilities of many clinics were inadequate, particularly as far as plaster casts were concerned. Delaying cast changes until the end of the clinic, because of personnel shortage, often caused hours of waiting. In some instances patients were given other appointments to return on special cast days, entailing an extra visit for the mother and child.

Operating rooms were well equipped, although frequently the operating suite did not have good facilities for extensive plaster work. Only two-thirds of the hospitals had qualified directors of anesthesia, and in only one-third was anesthesia routinely administered by qualified physician anesthetists. In several of the hospitals with approved orthopedic residencies, anesthesia was given routinely by nurses. In general, x-ray and laboratory facilities were good. In only 5 hospitals was there a unit system of records where clinic and inpatient charts were kept together so that there might be a continuity of medical information between in and out patient services.

Two other programs have been recently developed by the Bureau, namely, the medical evaluation of children being taught by home teachers, and those in special classes because of orthopedic handicaps. In both groups about one-third of the children were misplaced, and belonged in either special classes or regular classes, respectively. This educational misplacement of one-third of the orthopedically handicapped children reflects either lack of knowledge as to the types of school facilities available in the city, or an overprotective attitude toward handicapped youngsters, and represents another area where we are badly in need of help from both pediatricians and orthopedic surgeons.

It can be concluded, therefore, that there are real problems associated with the care of orthopedically handicapped children throughout New York City. Some institutions offer excellent over-all facilities, while others fall below the accepted standards of good care. The problem is posed as to the need for the further overextension of inpatient hospital facilities for orthopedically handicapped children in the light of the lack of demand for these facilities.

The more prominent areas requiring attention are in the development of better liaison between orthopedic and other related hospital services, particularly pediatric, physical medicine, rehabilitation, and social service. A separate children's orthopedic clinic, with pediatrician in attendance, routine pediatric and social service coverage of all orthopedic cases admitted, joint orthopedic, pediatric and physiatric rounds and conferences, and training of pediatric residents in orthopedic problems are suggested.

Overinstitutionalization can be reduced by improved general medical supervision, teamwork between the various services, and greater use of convalescent or, better still, social service and public health facilities to make interval home care more practical. Among other needs are integration and development of orthopedic residencies and their separation from general surgery, use of only qualified orthopedists on staffs, better planning and staffing of orthopedic clinics, and more careful attention to school placement recommendations.

The success of the over-all program to improve orthopedically handicapped children's care in New York depends upon the cooperation of all practicing physicians and hospital staff members dealing with the problems of the crippled child. It is the responsibility of the orthopedist and pediatrician to demonstrate the leadership and to interest and coordinate the other members of the team—the specialist in physical medicine and rehabilitation, the various therapists, the nurse, the social worker, and the hospital administrator—in order to assure to the orthopedically handicapped children of New York City and other communities the best over-all care that modern medical science can offer.

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COMMUNITY RESOURCES FOR THE CHRONICALLY ILL

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RECENT years have witnessed an extraordinary spurt in attention to the many-sided problems of the chronically ill. A flood of articles and professional studies have deepened the understanding of many disciplines: medicine, nursing, social work, psychology, nutrition, vocational counseling, rehabilitation, to name but a few. Since much of the recent literature has concentrated on understanding the needs of long-term patients, many unanswered questions have inevitably been raised about how to carry this understanding forward into an operating program. What is lacking, by and large, is a clear picture of the results of community effort to close the gap between known needs and available resources.

Since the general character of the needs of long-term patients is well understood, it is relatively easy to draw the outlines of necessary community services. It is, therefore, all the more frustrating not to know whether our social institutions are really responding to these known needs and proposed plans. How are social institutions such as hospitals and social agencies responding to the accumulated knowledge? What obstacles have been encountered in planning? After all, hospitals, chronic institutions, homes for the aged, and social agencies are the social devices through which most organized service for the chronically ill is delivered. Their actions determine how far knowledge is translated into daily practice for patient benefit.

The Council of Jewish Federations and Welfare Funds has, for several years, assembled information about program developments in general hospitals, institutions for the aged, and family service agencies under Jewish auspices. Beginning in 1949 a series of special studies† was initiated which brought together much useful data on the ways in which institution and agency practice are re-

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†The studies referred to include: (a) a 1950 study of reports from 46 Jewish institutions for the aged about characteristics of their resident population; (b) a 1952 study of medical expenditures in 39 institutions for the Jewish aged serving any chronically ill patients; (c) a 1954 descriptive study of home medical care plans initiated by 9 of 41 Jewish general hospitals covered in the inquiry; (d) a 1954 study of cooperative plans developed by 41 Jewish general hospitals with nearby long-term care institutions; (e) a 1953 study of program developments in 63 Jewish family agencies. These special studies were designed to secure specific data supplementing general service statistics reported annually by these agencies.

In each study a schedule was designed to secure limited data; was distributed to all regularly reporting agencies; and returns analyzed against annually submitted data. The percentage of responses was uniformly high, well over 90 per cent.

sponding to known needs. The reported data give encouragement about the adaptability and flexibility of our social and health agencies. Several major findings are summarized here.

Although progress may have to be measured in years rather than in months, it is possible to conclude that articles, conferences, and scientific studies do find their way into the daily practice of institutions which care for the chronically ill.

Before reviewing these developments, two over-all factors need mention. First, the physical care and social well-being of long-term patients require as much attention as does the phase of active medical treatment. The medical professions seek facilities for decent physical care of patients as earnestly as custodial institutions seek their better medical care. Recognition of the interdependence between these aspects of chronic disease has led to a deeper understanding on the part of physicians and other disciplines.

Second, the social agencies referred to do not conform to the stereotype of welfare agencies. In general, they serve all economic and social classes. Like hospitals, with 85 per cent of the patients paying their own bills (with the help of insurances), family service agencies have about 70 per cent of their clientele economically independent, and homes for the aged, with the help of the social security program, care for a high proportion of economically independent residents.

These agencies may well be viewed as the instrumentalities by which various professional services are made available to all strata of the population.

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INSTITUTIONS FOR THE AGED

Institutions for the aged are rapidly becoming a major resource for care of the long-term patient. This is of great significance when we recall how pressing is the demand for facilities to provide physical care accompanied by decent medical attention. Only a few years ago, these institutions were viewed as residences for retired, well, ambulant old people. Their application and admission policies, in most instances, specifically excluded sick or handicapped persons.

In 1950, a preliminary study of 46 institutions for the Jewish aged in cities of all sizes reported nearly all residents as chronically ill and between one-third and one-half placed in infirmary beds. In the aggregate, 33 per cent were completely bed or room bound. The occupancy totals are shown in the accompanying table.

NO. OF INSTITUTIONS	TOTAL RESIDENTS 12/31/50	TOTAL INFIRMARY BEDS	RESIDENTS CONFINED TO			RESIDENTS EXPECTED TO BE BEDRIDDEN OVER 3 MONTHS
			WHEEL CHAIR	ROOM	BED	
46	3,991	1,051	202	813	296	238

A follow-up study in 1952 threw new light on the rapidly changing situation. Of 39 reporting institutions, 20 were licensed by a state agency as a medical institution other than a hospital. In 19 instances, they admitted nonambulatory and seriously ill patients if they were not in need of care in a general hospital; and three others admitted such applicants in exceptional cases. Since that time this practice has spread to other homes. At a minimum these institutions have become the community-supported counterpart of the commercial nursing home.

A further attempt was made to determine the type of care given these sick and bedridden residents. Since uniform cost accounting methods have not yet been developed, 29 institutions were asked to report the amounts expended in 1951 for medical services for their residents. These medical expenditures were defined to include only: physicians' salaries, nurses' salaries, medications, and hospitalization. The reported figures understate the situation by excluding contributed physician services, free hospitalization secured from a nearby general hospital, and other ancillary and diagnostic medical expenditures.

With this orientation, institution expenditures for medical care averaged between 20 per cent and 30 per cent of total receipts (which equal total expenditures in most cases). These costs ranged from a low of 8.4 per cent to a high of 43.6 per cent of total receipts. In institutions with the most extensive medical care, the estimated per diem cost in the infirmary is between $8.00 and $10.00, which approximates chronic hospital costs, and yet is substantially below costs of care in a general hospital.

It can be concluded fairly that these Homes for the Aged have become quasi-medical institutions; many are rapidly becoming full medical care institutions for the chronically sick, although they are not classed as hospitals.

This recent development has serious implications for community planning. Such questions as these need to be asked by the medical profession as well as by social workers and community planning bodies: How far should custodial institutions go toward becoming medical agencies? What noninstitutional services can be adapted to care for the less seriously ill and handicapped patient? What types of medical and social service staffing is desirable to assure adequate care for residents? What should be the relations between this staff and that of hospitals and other agencies? Answers are in the making in many communities and no pattern is yet clearly discernible, although professional opinion has been often expressed. Some examples of "patterns in the making" are noted in the next section.

GENERAL HOSPITALS

Hospitals and their staffs have always treated chronically ill patients, although in recent years their attention has been directed mainly to short-term care of long-term patients. Despite this emphasis, most general hospitals find themselves treating an unspecified number of patients 30 days or longer because no adequate alternative facility can be found, even though a general hospital bed is not required by the patient's condition. Some local studies have placed the number of hospital days' care for these patients as high as 20 per cent of total days' care.

Two developments among general hospitals under Jewish auspices bear on the problem of long-term care: home medical care plans and cooperative relationships with custodial institutions.

In the past four years, nine of 41 general hospitals under Jewish auspices have initiated home medical care programs with their own staffs. By and large, these have been used for chronically ill in-patients of the sponsoring hospitals who require extended care under close medical supervision. The patients selected for these experimental projects have all had adequate homes of their own where care could be given with the help of visiting nurses, social workers and homemakers to supplement the medical supervision of family or visiting physicians.

These projects are in the pilot stage only. The number of patients cared for are very small; under 500 annually in nine hospitals whose bed capacity totals over 3,500. Staff requirements have not yet been established. Criteria governing the types of medical conditions best served have not yet been devised. Despite this, recent studies of these programs indicate their potential value does not lie in reducing demand for general hospital beds. The real value seems to lie in the use which doctors, social workers, and nurses can make of home care plans to learn better the many-sided needs of long-term patients. These needs are interlocking and changing. The success of these programs depends upon uncompromising attention to all needs or patients cannot remain in their own homes. Thus many disciplines are required to learn from each other about ways to secure comprehensive medical care. Aside from education, home care has by now proved that general hospital resources can be taken outside the hospital walls for the extended and expanded treatment of long-term patients.

Another general hospital effort to extend its usefulness involves cooperation with a long-term care institution such as a Home for the Aged. A study of local practice indicates that at least 12 Jewish general hospitals have extended their facilities and professional staff to improve medical care for residents of Homes for the Aged and other long-term institutions. The methods developed are varied. These are some illustrations:

a. The directors of a few hospitals appoint, from their visiting staffs, a physician to be employed by a Home for the Aged as its medical director.

b. In some hospitals, arrangements are made to rotate a resident physician who will live in another institution for several months and attend to the medical needs of the residents under the supervision of a medical director.

c. In several cases, medical specialists, occupational therapists, nurses, social workers, or dietitians of a hospital are used by other institutions as consultants on special problems of caring for the chronically ill.

d. In a few cases a hospital arranges for comprehensive medical and diagnostic work-ups annually for all Home for the Aged residents, usually through a geriatrics clinic backed up by hospital admission where necessary.

e. It is common practice for a hospital's special laboratory, diagnostic, and surgical facilities to be made available to aged institution residents and their physicians without charge to the institution.

The result of these and related arrangements is to pool medical resources under hospital standards; to bring better medicine into many institutions; and

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to minimize the necessity for building duplicate medical facilities. There remain to be developed more effective means by which hospital and long-term institution beds can be used interchangeably with greater ease. It is still too difficult to transfer a patient from an institution for the aged to a hospital; and almost impossible to transfer a hospital patient to a Home for the Aged (unless he was formerly a resident there). This development holds much promise for community health. Physical facilities and skilled personnel can be brought together more flexibly; capital needs can be kept to a necessary minimum; and medical care can be improved by wider use of skilled professional people in places hitherto lacking adequate staff.

FAMILY SERVICE AGENCIES

At the turn of the century, many family agencies provided physician and nursing services to the underprivileged. As hospitals developed their program, family agencies first concentrated on relief and other social services. Since 1935 they have given major attention to problems of family and personal adjustment.

In this period a gap has developed between these agencies and medical institutions, with the family agency tending to refer all medical or medically related problems to a medical institution without retaining much responsibility for joint or cooperative activity.

Since 1950, a number of developments have demanded family agency attention to some aspects of chronic illness. A primary influence has been the increase in numbers of people over 60 years of age coming to these agencies with medical and health problems prominent in their requests for service. In 1953, 23 per cent of the caseload of 63 Jewish family agencies involved care for people over 60 years of age. Agencies began to respond to this change in community need by providing some or all of these services: physical care in the patient's home, information and referral about resources, and prevention through personal counseling. Many of these services are needed by and can be provided to younger chronically sick patients as well as the aged.

Among 63 Jewish family agencies in cities of all sizes, included in this survey, over one-third offer homemaker or housekeeper services to older people for varying periods of time which enables them to live at home with illness or disability. Much of this service assumes full household responsibility for short periods of time only. Agencies in New York and Chicago are now committing a few housekeepers to part-time service for older people over indefinite periods of time.

Another one-third are responsible for locating and supervising special boarding homes in which older, and often ill, clients can live in a home environment when they are no longer able to maintain their own homes. Unfortunately only a few of these are screened for suitability for very sick people. Only the Jewish Community Services of Long Island maintains a comprehensive boarding program supported by active medical leadership.

In two-thirds of the agencies, some help is offered to secure nursing care. The nature of this service may be limited to a central register of approved board-

ing homes. In a few cases commercial nursing homes are studied in an effort to raise their standards of care. In one case a family agency administers a community nursing home. In almost all cases financial help to secure nursing home care for short periods of time is provided if other resources are lacking. The agency maintains regular contact with the commercial nursing homes to help them raise the level of services provided. For example, casework and recreational or occupational therapy services have been improved, or brought into cooperating homes.

Almost all reporting agencies keep data about available resources for sick people to help patients or applicants find the resources best suited to their needs. This may involve close cooperation with hospitals, nursing homes, boarding homes, rehabilitation centers, and sheltered workshops.

Much of this information has, in the past, been sketchily evaluated, and available services were not linked closely to problems of the chronically ill. The rise in applications from persons in this category has required more specialized attention. In Chicago, for example, the Jewish Family and Community Service now serves as a central intake service for older people seeking all forms of help. All resources—medical, social, psychologic, and custodial—are drawn upon to evaluate requests and consultation is given about appropriate resources. This activity also serves to bring hospitals, the family agency, and custodial institutions closer together to pool their experience and to plan jointly for unmet needs. This type of service can, in part, fulfill the function performed in other communities by independent Central Services for the Aged or the Chronically Ill (New York, Chicago, Milwaukee, Newark, Cleveland, and San Francisco).

Such central information and counseling offers a real hope for translating professional knowledge about prolonged illness into client and patient care.

A wide cross-section of individuals and families come annually to family agencies for information and consultation. A sensitive reception to health, or health affected problems can help identify them early so that prompt remedial or preventive measures can be taken.

The potential role of these agencies in meeting some long-term needs seems very great, but specific developments are difficult to identify. Some of the difficulty may lie in the absence of close working relationships between physicians and social workers at a hospital and those working for a family agency. Another obstacle lies in the diversity and diffused character of problems coming to these agencies for help. The potentional value of greater medical-social collaboration between these agencies and medical institutions lies in the great preventive and diagnostic opportunities to be found in the normal client group using a family agency.

The Boston Beth Israel Hospital and Jewish Family and Children's Service is planning a collaboration which may bring useful results. Between 100 and 150 clients of the family agency are over 60 years of age. Little is known about their total medical needs. The medical staff of the hospital has agreed to use its resources to conduct comprehensive evaluations of all of these clients for whom

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it is appropriate. The evaluation will include physical, social, psychologic, and emotional findings. The results can be useful to the clients and to professional staffs of hospital and agency in determining what services are required.

SUMMARY AND CONCLUSIONS

Several conclusions can be drawn from the special studies here reviewed:

1. Institutions for the Jewish aged have radically changed their functions and programs in recent years, and have greatly expanded their medical and custodial services for the chronically ill.

2. General hospitals have begun to use their professional resources more flexibly to raise the level of care for long-term patients outside of a hospital bed through extension services to long-term institutions and home medical care plans.

3. Family service agencies, working with individuals in their own homes are confronted with an increasing flow of social problems resulting from chronic illness and disability. They are increasing the variety of their services, but the volume is still small, and relationships with medical agencies are often casual or remote.

4. Organized services for the chronically ill outside of institutions are developing much less rapidly than programs within institutions.

5. Collaboration between agencies is less advanced than is collaboration, on a teamwork basis, among professional personnel working within single agencies.

These developments indicate the different ways these types of social institutions have responded to changing needs and how ready they are to apply new knowledge.

These changes make new demands for coherent community planning between citizen groups, medical, social work and related professions, and community agencies. Advance planning may result in better service for more people. Lack of planning may result in competing building plans and isolation of various professional bodies from each other as they work with the same groups of patients.

It is interesting to note that, contrary to general opinion, services outside of institutions have changed less rapidly and with greater difficulty than have institutions such as Homes for the Aged. This may be due to the greater diffusion in service demand of noninstitutional programs. However, since they are not hampered by buildings, greater interprofessional collaboration may result as soon as the advantages are recognized.

It may be argued that the agencies covered in these studies are neither typical nor representative of all services for the chronically ill and that they may represent too optimistic a picture of change. Without claiming representativeness, these agencies and hospitals do include a wide range of forward-looking as well as conservative and slow-moving institutions. Their experience, when viewed overall, suggests how much effect the concentrated discussion of recent years has had and can continue to have.

The ferment of new knowledge is at work, and social institutions are clearly responding in ways which cannot help but encourage all who are concerned with better care for long-term patients.

SELECTING AGED PATIENTS FROM MENTAL HOSPITALS FOR CARE IN CHRONIC HOSPITALS

Review of Experience in Connecticut

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INTRODUCTION

WIDESPREAD belief that many aged individuals have been committed to mental hospitals for want of more suitable facilities has been responsible for concerted attention to this one area of care of the aged. Motivation for this attention differed. Public-spirited citizens were desirous of sparing older persons the stigma of mental hospitalization, the mental hospitals saw an apparent opportunity to relieve their crowded conditions, and various groups concerned with chronic illness saw an apparent opportunity to develop facilities and program specifically to meet the needs of these senior citizens.

Many plans and predictions were made on the basis of preconceived notions as to the nature of the problem. The Connecticut Commission on the Chronically Ill, Aged and Infirm published plans developed for one of its units[1] which now must be modified in the light of recent findings. There has been a popular impression that an aged person who has outlived his relatives and no longer has sufficient sources of income to live independently, and who has become slightly confused, is sent to a mental hospital because no one else will care for him. Consequently it was thought that this type of patient was crowding the mental hospitals to the detriment of younger patients who might benefit from active psychiatric care and was himself being denied appropriate care.

This impression was strengthened by the fact that in Connecticut 40 per cent of the State mental hospitals' population is 60 years of age and over and 34 per cent of new admissions to these hospitals are likewise 60 years of age and over. However, Connecticut is in an unusually healthy situation in so far as both availability and high standards of its health and welfare programs and facilities are concerned. Awards to the 16,791 Old Age Assistance clients in Connecticut are second highest in the nation.[2] Standards for private nursing homes are among the highest in the nation, with 5,882 beds in these facilities which are licensed as chronic and convalescent hospitals.[3] In addition, there are some 3,454 beds in licensed boarding homes and church and fraternal homes for the aged,[4] 1,330 beds in town facilities,[5] as well as a 1,250 bed Veterans' home

and hospital caring for many older veterans. These facilities serve a population of 2.27 millions.[6]

Although it may be true that in some states lack of these facilities may cause admission to mental hospitals, data recently obtained in Connecticut, by the Commission on the Chronically Ill, Aged and Infirm in cooperation with the State Department of Mental Health, do not support the existence of this condition in our State.

THE CENSUS STUDY

The first of recent studies of patients in Connecticut's mental hospitals was concerned with the numbers of aged persons in the institutions on specific dates during the fall of 1954, who might be suitable for transfer to a chronic hospital. A detailed analysis of this study is presented elsewhere.[7]

Because of the lack of precision in the term "senile," and the similar lack of precision in the simple statement that many "senile" patients do not belong in mental hospitals, definitions and criteria were developed prior to the actual review of cases. Since the patients being studied were in the mental hospitals, the diagnoses recorded by the trained staffs at these institutions were used for the purpose of this study.

Any patient who was diagnosed as having cerebral arteriosclerosis or senile brain disease was included in the group called "senile." Many such patients had, coupled with this diagnostic designation, the additional problem of "psychotic reaction." It is evident that a diagnosis of "senility" is not synonymous with absence of mental illness.

In attempting clarification of the statement that these persons do not belong in mental hospitals, a series of questions concerning behavior manifestations was employed in selecting patients for possible transfer to one of the chronic hospitals operated by the Commission on the Chronically Ill, Aged and Infirm. To persons untrained in psychiatry, affirmative answers to these questions seemed to preclude care in other than a psychiatrically supervised setting. The questions asked were as follows:

Is the patient a suicide risk?
Is the patient an escape risk?
Is the patient abusive or profane?
Is the patient assaultive or destructive?
Is the patient deliberately noisy to the discomfort of others? Does the patient exhibit any bizarre eating or toilet habits (excluding involuntary incontinence)?
Is the patient unable to comprehend simple instructions?
Is the patient unable to communicate his basic needs?
Is the patient unable to adjust to the simple demands of institutional life such as keeping on his clothes, taking baths, etc.?

In addition, obvious symptoms such as hallucinations, delusions, and the like were grouped as miscellaneous manifestations.

Before selecting actual cases to be reviewed, the total census of the three mental hospitals was determined. Of the 10,289 persons on the hospitals' census as of specific dates, 4,178 (40.6 per cent) were 60 years of age and over. A 10 per cent sample of those 60 years of age and over was selected at random by the use of standard tables of Random Numbers. The definitions and criteria described were then applied to the 417 patients in the sample.

Only 150 (36 per cent) of the study sample were diagnosed as "senile" by the mental hospital staffs; the remainder had diagnoses of other types of mental disease. Most of the latter group had been admitted when young and had simply grown old in the mental hospitals. Just as the mere attaining of the age of 60 by a normal person does not make him "senile," the attaining of the age of 60 by a mentally ill person does not convert his mental illness into simple senility.

Of the 150 "seniles" in the sample, 101 showed one or more of the behavior problems listed above, some having as many as six or seven of these problems concomitantly. The average among these unsuitable patients was 3.63 behavior problems per patient. Because a patient may actually be "psychotic" even though he displays none of the obvious manifestations listed above, an additional 9 patients were considered by the mental hospitals as poor risks for transfer. Further, 17 patients on the census who meet the criteria were not available for transfer because they were on leave or in convalescent hospitals. Thus only 23 "senile" patients in the sample were found who might make an adjustment in a chronic facility and were available for transfer. However, 7 of these failed to make the expected adjustment after actual transfer to a chronic facility and had to be returned to the mental hospitals.

Our random sample represented 10 per cent or 417 of the 4,178 patients 60 years of age and over in State mental hospitals in Connecticut. Applying the sample proportions to the entire group of 4,178 patients in the 60 years of age and over group, it is found that only 161 (1.56 per cent) of the total hospital census may be considered as "senile" patients who are acceptable for continued care and treatment in facilities other than mental hospitals. Measurement of the reliability of the sample percentage indicates that there is a 95 per cent fiducial probability that the true number of these patients would not exceed 3.11 per cent of the total hospital census and a 99 per cent fiducial probability that they would not exceed 3.77 per cent of all patients.

THE ADMISSION STUDY

A further study of patients admitted to the three mental hospitals during the months of October, November, and December, 1954, was performed early in 1955, using the same definitions and criteria developed for the census study. Eight hundred thirty-four persons were admitted during this period, of whom 287 (34.4 per cent) were 60 years of age or over. Only 203 of these were "senile," the others having diagnoses of other mental illness. In the rare case it might be said that circumstances justified question as to the necessity for admission. Only 3 persons were discharged within 30 days (the period of emergency admission[8]) as noncommittable.

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To determine the validity of the statement that it was lack of other facilities which prompted admission, the source of patients was recorded at one of the mental hospitals. Sixty and eight-tenths per cent had come to this institution from either a general hospital or chronic and convalescent hospital (nursing home), and it was evident from information supplied by these facilities that inability to cope with manifestations of mental illness prompted the patients' admission.

In analyzing the effect that these newly admitted "seniles" have on crowding in the mental hospitals, it was found that about half (101 out of the 203) did not receive care for any appreciable length of time. There were 75 deaths, 18 discharges, and 8 patients who were able to return home on extended visits all within a relatively brief period. The range for deaths was from 3 to 180 days from the day of admission (39 patients died within the first 30 days, 11 between 31 and 60 days, 20 between 61 and 90 days, and 5 between 91 and 180 days) with a median of 27 days for the group. The range for discharges and extended-leave patients was 9 to 146 days from the day of admission and the median for these 26 patients was but 53 days.

It has been suggested that the 75 who died must have had physical illness and, hence, might well have been candidates for admission to a chronic facility. The data indicate that at one mental hospital, 63.3 per cent of those who died had been admitted to the mental hospital either from a general hospital or a chronic and convalescent hospital. In only 6 of those who died was there any evidence to indicate that their admissions to a mental hospital might have been prompted by reasons other than serious emotional disturbance or unmanageable behavior.

Of all the admissions reviewed, 19 "senile" patients were considered suitable for transfer to facilities of the Commission on the Chronically Ill, Aged and Infirm. These were patients in whose behavior improvement was noted within an average of three weeks of admission, and who apparently had been retained for continued observation. In many instances discharge from the mental hospital would have occurred regardless of selection for transfer to a Commission facility. Since the experience in the census study showed that the patients retained by the mental hospitals and those who must be recommitted after transfer account for about half of the apparently suitable cases, the estimate of the number of patients who may be expected to receive continued care in a chronic facility probably does not exceed 10.

There remained 83 newly admitted patients who were deemed unsuitable for transfer, employing the same criteria used in the original study. Eleven of these were patients whose behavior had necessitated their commitment to the mental hospital from either Undercliff Hospital or the New Britain Memorial Hospital, two facilities under the jurisdiction of the Commission on the Chronically Ill, Aged and Infirm. All 83 patients still displayed many of the symptoms which were present on admission. The persistence of symptoms after an average of three and a half months' observation may be contrasted with the rapid change noted in the cases deemed suitable for transfer.

The number, therefore, who may be expected to improve to the point where transfer may be considered does not appear to be appreciable. The findings reported here indicate that about 1.2 per cent of the admissions can be described as "seniles" who may feasibly be cared for by personnel not trained in psychiatric management.

Thus it would seem that the so-called "senile" does not constitute any special problem in Connecticut's mental hospitals, except that any patient requiring continued psychiatric supervision drains the resources of an already crowded and understaffed facility. Also, the younger mentally ill person is usually physically healthy and able to contribute to his care by performing supervised tasks. This accomplishes the dual purpose of providing therapeutic activity for the patient and helping to reduce personnel needs for the nonprofessional aspects of operating the institution. The older patient with mental illness too often is physically incapable of being placed on useful activity and is not in the same position of being able to benefit from such therapy. In these aspects he may well be a special problem.

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"SENILES" COMPARED TO AGED PATIENTS WITH OTHER DIAGNOSES

The "seniles" who can be cared for in other than psychiatrically supervised settings appear to be no different from other patients who reach a point where a reasonable risk may be taken in giving care outside a mental hospital. As a follow-up to the studies described above, patients placed by one of the mental hospitals in a private chronic and convalescent hospital were reviewed. These were patients in both the "senile" and other diagnostic groups. In this one facility, as of a specific date, 57.7 per cent of the cases placed were within the "senile" classification and the remainder had other diagnoses in the mental hospital records.

In the census study of patients 60 years of age and over in the mental hospitals, there was found to be another group, not "senile," who might be cared for in a nonmental facility. This group was about equal in numbers to the "senile" group. Cases selected and referred by the mental hospitals for transfer to a chronic nonmental facility were reviewed. Again the "seniles" accounted for only 57.5 per cent of the group. Of the patients actually admitted to undercliff Hospital as a result of the surveys and referrals by the mental hospitals, 53.8 per cent were "seniles," the remainder having other psychiatric diagnoses. It should be borne in mind that there are approximately twice as many "not senile" patients in the study sample. The numerical equality of the two groups found to be suitable for care in a nonpsychiatric setting, therefore, represents twice as great a percentage among the senile group.

The use of facilities other than mental hospitals to care for the relatively few suitable cases, as an expediency to help relieve crowding, has therefore met with equivocal success. While it is true that a significant number of cases are under care, many show frank psychiatric problems which cannot be supervised adequately by nonpsychiatrically trained personnel. Evidence that this is the case may be found in the fact that while only the more obvious and flagrant

behavior problems have occasioned recommitment to the mental hospitals from Undercliff Hospital, 17.1 per cent have had to be recommitted to date, and many more should be under psychiatric supervision, in the opinion of a local psychiatrist.

Even in the program of placement in private convalescent facilities instituted by the mental hospitals, an appreciable return rate has been experienced. Ninety-five patients, still on the mental hospital census and remaining under the jurisdiction of the mental hospital, were placed in one such convalescent home because of their expected ability to make a good adjustment outside the mental hospital. Twenty per cent of these required return to the mental hospital because of behavior problems; an additional 15.8 per cent were returned for investigation and treatment of medical conditions, in accordance with a prior arrangement made with the mental hospital before placement of the patients. It must be emphasized that these are special cases in which the patient is in the convalescent facility as a parolee from the mental hospital and is carried on the mental hospital census. These cases are not included in the new admissions reported above.

Information derived from our studies in Connecticut is supported by data on mental hospital utilization gathered by the National Institute of Mental Health, Public Health Service, U. S. Department of Health, Education, and Welfare and reported in various publications. The following is an example:

> There are marked differences between the diagnostic distribution of resident patients and of first admissions to State mental hospitals . . . . The proportion of schizophrenics is almost twice as high among patients as among first admissions. On the other hand, the proportion of patients with mental diseases of the senium is more than twice as high among first admissions. Admissions of senile cases have increased greatly in the last decade, but the population of most mental hospitals consists largely of a slowly accumulated residue of schizophrenic patients who are admitted during youth or early maturity and stay, in many cases, for the rest of their lives. The turnover of senile cases is very rapid because of their high death rate . . . .[9]

Likewise, the following summary[10] of the factors contributing to the growth in mental hospital population lends credence to the findings in Connecticut:

1. The general population has grown. There are simply more people who could have a mental disease.
2. There are more people in the older age brackets, where the highest incidence of mental disease has always fallen.
3. More hospital accommodations are available for care and treatment of mental patients. In the past, additional accommodations have always meant additional patients because the need for accommodations has been so great.
4. Both the medical profession and the general public know more about mental disease, and have been increasingly willing to utilize mental hospitals. Confidence in the hospitals has grown.
5. The concept of mental disturbance has broadened. Formerly, only the severest types of mental illness were considered for hospitalization, but patients are now drawn from a wider and wider range of disturbed conditions.

6. People live longer, not only in the community but in the hospital. They have a greater average duration of hospital life, partly because of improved standards of general accommodation and care that prolong life itself. Some patients, too, remain longer in the hospital because of higher standards of psychiatric care, because of the inability or unwillingness of the community to find places for them, or because of the shortage of social workers for aftercare.
7. Urbanization of society is doubtless a factor. Many mentally erratic or disturbed persons, who might be cared for quite well in a farm or small-town environment, may be both helpless and difficult in a crowded urban center. Mentally ill persons, especially the aged and senile, are all too often an unbearable burden in a city apartment. Moreover, the rushing tempo of urban life today is a far cry from the typical living conditions of a century ago. This *may* act to produce more disturbed people; it *does* act to make it more difficult for the disturbed person to get along in the world outside the hospital.

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CONCLUSIONS AND SUMMARY

The data presented indicate that a program for discharge of patients to nonmental facilities has a number of limitations as a permanent solution to the problem of the "seniles," or even the nonsenile older persons, in Connecticut's State mental hospitals. Essentially, the indications are:

1. That persons 60 years of age and over are sent to mental hospitals in Connecticut because of the presence of mental illness.

2. That the majority of the persons 60 years of age and over in Connecticut's mental hospitals have diagnoses other than "senility" and are persons who have grown old while under care in the institutions.

3. That newly admitted older persons enter Connecticut's mental hospitals because other facilities cannot provide the necessary psychiatric supervision.

4. That the small but significant number of both "seniles" and patients with other diagnoses who are apparently reasonable risks for care outside Connecticut's mental hospitals represent simply the normal discharge problem of any type of institution.

5. That the attempt in Connecticut to transfer patients who are truly in need of psychiatrically trained personnel for appropriate management, even those not displaying flagrant behavior problems, has met with limited success. This appears to be true regardless of the resource used, indicating that only a mental institution can adequately manage these cases.

While there is much current emphasis in this state on programs to meet the needs of persons disabled by virtue of chronic physical illness or infirmities of age, this does not mean that these programs can meet all the problems which face a person who has reached advanced years. In the same way that mental hospitals must meet the medical and surgical problems of their younger mentally ill patients, they alone would seem to be the facilities to meet the physical needs of the older mentally ill patients once they have reached the point when our medical profession recommends admission to our mental hospitals.

The removal of elderly mentally ill persons from mental hospitals to institutions less suitably equipped to handle their problems may seem to provide a ready solution for crowding in the mental institutions. The more intelligent and humane approach would seem to be a concerted effort on the part of all involved in this field of activity to work for more adequate mental hospital facilities and programs which would give the increasing number of mentally ill persons the type of service they require, regardless of age.

There remains much to be done in the early stages of "senility." Efforts must still be directed at programs designed to prevent mental deterioration and to render service to older persons who have not yet reached the doors of our mental hospitals. However, wholesale transfer of elderly patients from mental hospitals to other types of institutions does an injustice to two fields: i.e., the programs concerned with the needs of our aged and those concerned with our mentally ill.

It is an unfortunate development at this stage in our efforts—while interpreting mental illness as illness carrying no greater stigma than physical infirmity—to segregate a group of persons simply because of age as inappropriate to receive care in our mental institutions. Nor does it seem appropriate to modify our programs designed to meet the specific needs of people, which needs may be more prevalent as age increases, by having separate groups design separate programs to meet the needs of mental illness in our older citizens. Is there a greater difference between the aged who are mentally ill and any others who are mentally ill, than there is between the aged with reduced financial resources and other persons with reduced financial resources?

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PSYCHOTHERAPY OF THE NEUROTIC AGED

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WITH the shifting of the age distribution in the general population, the physician has been forced into a new field—that of the care of the aged, who are commonly designated as persons "over 65." In actual numbers this "aged" group has quadrupled within the first half of the century. Between 1930 and 1940 the increase was five times that of the general population. In the next twenty-five years we may expect the group to double in size again.

The problem this presents for those concerned with the care and treatment of patients suffering from emotional disorders is reflected in the increase of first admissions to mental hospitals from this group. This has risen from 13 per cent to 38 per cent. Actually, the increase in admissions to mental hospitals in the past thirty years has occurred almost entirely in the "over 65" group. Mental hospital admissions serve as an index to the problem of emotional disorders of the aged in its severest form.

When the preponderance of the aged among those afflicted with chronic disease is considered, most physicians will admit to the growing numbers of the aged in their practice and the problems which they present. It is estimated that 19 million persons suffer from some form of chronic disease, and the commonest illness responsible for chronic disability in the general population (all ages) is arthritis.

Home visiting services report that the aged now constitute about one-third of their case load. However, many of these are homebound because they are too emotionally disturbed to be cared for in general hospitals. The practicing physician is not too sensitive to this problem, because it occurs at the periphery of his professional interest. He feels that medical care of the aged is essentially the palliative relief of pain, and he adopts a "hands off" attitude in his treatment of the aged whose loss of function and ultimate dependency he regards as inevitable concomitants of old age. Our responsibility as physicians should not end there, but should assist the patient in making an orderly transition to an occupied, if not productive, old age. Equally as important as healing the sick, though possibly less gratifying, is the relief of suffering.

Among the aged are many whose emotional problems trigger clinical manifestations of a somatic illness, aggravate the disease process, or interfere with otherwise effective treatment. The "neurotic" aged usually present themselves primarily with somatic complaints and great concern over their physical state.

The latter proves to be the most refractory problem in their management. Inquiry reveals many difficulties in their life situations which cannot be readily altered, which explain feelings of resentment and depression. Further probing often reveals a history of social and sexual maladjustment. The possibility of psychiatric help is usually not considered because the patient is thought too old to change, even though the emotional picture is recognized as a causative factor in the somatic illness. However, the same condition, in a younger patient, would lead to a psychiatric referral.

It is the purpose of this paper to indicate the feasibility of psychotherapy in the "neurotic aged."

CASE M.R.—A 72-year-old married woman was referred to the psychiatrist because of severe cramps in the left lower quadrant, of two years' duration. Hospitalization totaling three months for investigation and relief of pain did not reveal an organic basis for the symptom, which was controlled with sodium Amytal 0.12 Gm. four times a day. Both the urologist and the internist felt that the pain was not related to a severe chronic interstitial cystitis which flared up every few months, with severe frequency and hemorrhage.

The patient admitted that she was depressed. She was living with her 75-year-old husband (a retired physician), who was showing a typical picture of senile deterioration—being forgetful, demanding, insulting, and then tearful. One son living at home had recovered, with defect, from paranoid schizophrenia and was easily upset. There was another schizophrenic son in a State hospital and a married daughter recovered, with defect, from two attacks of paranoid schizophrenia. The patient stated that when she went to the movies she forgot her troubles and her pain ceased.

Her symptoms first occurred shortly after the family finances were consolidated. Her husband for the first time checked the household bank statements and would rage at expenditures. Previously, the patient had supported the household with her independent means.

She was seen once a week for nine months. The depression and cramps improved after the expression of rage against her husband. Her condition continued to improve as she was helped to realize that her husband's behavior and his criticism of her were not valid, but derived from his emotional disturbance. With the rise of self-confidence and belief that she was an effective person who discharged her responsibilities adequately, her tension improved and sedatives became unnecessary. "I feel free for the first time in my life," she said.

In the past year, the patient has been seen once a month, and weekly during crises. These have consisted of another psychotic attack of the daughter; borderline psychotic attack of the son; the patient's own severe attacks of acute cystitis, with one severe hemorrhage; and national notoriety of a son-in-law, previously her favorite.

The husband's condition continues to decline. The patient reacts to these crises with depression and some guilt not of unusual severity, but cramps recur only occasionally for a few hours.

Comment.—Life-long emotional patterns of submissiveness and lack of self-assertion existed. The patient also had severe physical illness and a difficult life situation with which to contend. Improvement occurred when the therapist helped the patient to express her guilty rage at her husband's behavior, admit his mental illness, and gain greater control over her life situation with increased self-pride over her performance as a wife and mother.

The general impression of the emotional problem of the aged is that of the senile personality changes as described by Horace:

> Inert, irresolute, his neck he cranes,
> Into the future, grumbles and complains,
> Extols his young years with peevish praise,
> But rates and censures these degenerate days.

Most literature on psychotherapy of the aged reveals general pessimism because of the increasing rigidity of personality in old age, the diminished sources of gratification due to physical loss of function, and the environmental factors. Abraham,[1] and, more recently, Wayne,[2] Gitelson,[3] Mittelman,[4] and Rockwell[5] feel that "the prejudice that old individuals give poor psychotherapeutic results is unjustified."[4]

The capacity of a person to respond to psychiatric treatment is no more altered by age than is his response to antibiotics. The factors of age and chronicity are merely two of many that determine the outlook.

The theoretical approach to emotional maladjustment on which I operate therapeutically is an adaptive operational concept which has been outlined by Dr. Sandor Rado.[6] The individual has certain desires he is seeking to fulfill, and this motivation gives meaning to his constant interaction with the environment—Freud's emphasis on goal-seeking. The biologic needs of the individual are such that satisfaction usually results in greater fitness in the struggle for survival—a ceaseless struggle in every living thing. Adaptation to the struggle for survival is a frame of reference, a way of organizing the observed phenomena.

When there is frustration of the desires of the individual—be they pleasure or physical needs—emergency behavior, with its attendant emotions of fear and rage, comes into play. In a person with an infantile, overdeveloped conscience leading to neurotic inhibition and a sense of inadequacy, any difficulty in controlling the environment is regarded as an emergency and, therefore, calls forth an overreaction described by Rado[6] as a disturbance in "emergency behavior." The understanding and management of this irrational fear and the consequent rage which wells up as frustration becomes too great are crucial. When these feelings cannot be expressed in thought or action, their repression creates the autonomic imbalance that aggravates pre-existing organic disease—the psychosomatic condition.

In the aged there are common factors, both physical and environmental, that stand between desires and their fulfillment that may bring "emergency behavior" into play. The deprivation of the satisfaction of useful work places great stress on the individual's capacities for a diversity of other interests and abilities that can be exploited to give substitute satisfaction. Economic dependence aggravated in overcrowded housing accentuates the feeling of uselessness in the aged. The common motivation in the aged is to achieve a feeling of usefulness and position in society in order to maintain a sense of adequate inner stature and, at the same time, to derive some sensual satisfaction with a failing physical apparatus. The aged become, in fact, more dependent and in need of help.

The aged person reacts to his increased dependency with frustrations according to his previous pattern. He may feel satisfied with his past performance

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and accept the help offered with a sense of having earned it. Maladjusted patients, with their unique sense of inadequacy, respond to this extra stress with their previous neurotic patterns, such as coercive rage, blaming the environment and tyrannizing it, trying to force the necessary aid, or pleading helplessness and obvious fear. Goldfarb[7] pointed out how transparent is the pattern of seeking help in the neurotic aged. In most aged-maladjustment, there is too much fear of retaliation to allow the expression of fear and rage. This is repressed, and thus creates the autonomic imbalance leading to the psychosomatic symptom.

The therapeutic procedure then aims at relieving the emergency emotions of fear and rage, thus restoring autonomic balance. Where the problem is predominantly one of expressing coercive rage, the therapist maintains a firm attitude against antisocial behavior, but encourages an expression of the rage, agreeing with the patient as to his helplessness and exploitation. The end sought is some alleviation of the patient's frustrated desire to attain a sense of security and mastery of the environment. If successful, the patient achieves a victory over the therapist by gaining some real or fancied concession, and his fear of retaliation is reduced. With this rise of self-esteem and control of the substitute parental figure (the psychiatrist), the fear and rage diminish. The sympathetic attitude of the therapist is interpreted by the patient as parental approval, and this seems to create an illusion of greater strength leading to increasing self-assertiveness. This is channeled by the therapist to achieve more mastery over the environment and to provide increased pleasure. In all cases, particular attention is paid to the patient's physical condition, and attempts are made to achieve as good a control over this as possible. The psychiatrist takes an active part in prescribing for the patient—a concrete sign of care.

Dependency in old age is a fact, and therapy is aimed at making this consistent with the dignity and achievement of maximum pleasure possible to the patient. One may compare the treatment of the aged who show impairment of function, to that of the severely handicapped of other ages. Both the help of others and the use of prosthetic appliances when necessary must be accepted by the patient. They are so accepted, if the patient recognizes that through this assistance dependency is lessened and his mastery over the environment is increased so that he can function as closely as possible to the pattern of his more fortunate compeers. In my experience, most patients can experience sufficient pleasure to end their days contentedly. As physical resources fail, less and less is needed to achieve sufficient satisfaction and insure internal and external homeostasis both physically and emotionally.

In therapy, interviews are brief, not more than thirty minutes, and usually not more than twenty to thirty weekly interviews are needed to achieve maximum results. In cases where there is severe organic disease with much pain, a poor unalterable environment, or a severe maladjustment, additional weekly, biweekly or monthly interviews (for an indefinite period) are needed to re-enforce the therapy.

This is not an attempt to give any statistical evaluation of the results of psychotherapy for the aged. I have found, however, that roughly 75 per cent

of all patients seen both in private practice and in the out-patient department of general hospitals can be helped. The following case is illustrative of some of the results.

CASE F.F.—A 66-year-old woman was referred by her internist because of severe colitis of five years' duration. Rest, diet, sedation, antibiotics, and vaccines had proved ineffective. When I first saw her, the patient was too fatigued to work.

She stated that she had been depressed most of her life, and this was worse now because she was unable to work and was living on capital. She dreaded the future because of the possibility of needing "charity."

Her husband had been killed in an accident six months after marriage, and the patient had brought up one son, now 28, with much financial hardship. The son was homosexual, very disturbed emotionally, and was running through his inheritance and not working. His recent dishonorable discharge from the Navy because of homosexuality particularly disturbed his mother. She lived alone in a hotel and had few friends.

The patient stated that at the age of 53 she had been very depressed, with fear of insanity, and had been treated by hypnotic suggestion with some relief of her irrational fears.

During treatment, the patient raged at her "in-laws" for never having allowed her to work. This had, she felt, left her with no useful skill in her old age. She expressed great guilt over her son's homosexuality. Acceptance of the therapist in the role of substitute-parent was one of the measures used to relieve her guilt feeling. The resultant rise of self-esteem lessened her rage against herself, as well as her "in-laws." The patient was seen once a week for twenty sessions, during which time both her diarrhea and her depression cleared up. She was able to find a job which rewarded her with a feeling of financial independence as well as a sense of satisfaction. Three years later, she is still well and working full-time as a housemother in a small college.

Comment.—The patient showed a long history of neurosis, a severe psychosomatic symptom, and a difficult life situation. Therapy was able to relieve her guilty fear over the upbringing of her son, and this led to a rise of self-esteem and the consequent disappearance of her somatic disability, so that she could work and become self-sufficient. She is free of depression and hopeful of the future for the first time in her life.

SUMMARY

Age and chronicity are not a bar to effective psychotherapy. The method is outlined and illustrative cases cited.

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PSYCHOSOCIAL FACTORS ASSOCIATED WITH RHEUMATOID ARTHRITIS

An Evaluation of the Literature*

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FOR many years some physicians have felt that psychologic factors are associated with the onset or exacerbation of rheumatoid arthritis. Beginning in the early twenties there were reports[25,37,38,42,43,46] that it was necessary to consider the effect of the psyche in certain bony pathologies, that loosened emotions incompletely expressed in action had an effect on the body, that emotional trauma, or the mental state, was associated with the onset of rheumatoid arthritis and that the psycho-physio-chemical reaction of the arthritic might be due to years of emotional conflict.

In recent years there has been an increase in studies concerned with the personality characteristics of arthritics, including emotional conflicts and psychologic defenses, and with environmental stress factors which are other than of a physical or biologic nature. Although thorough studies of this kind are still few in number, it may be important at this point to evaluate our knowledge about psychologic and social factors in rheumatoid arthritis so that future research may be more carefully planned. That is the aim of this review.

Material from the studies reviewed here has been grouped according to the following topics: personality characteristics and conflicts, social background factors, precipitating factors, mechanisms, and rheumatoid arthritis and schizophrenia. An evaluation section follows each topic. Suggestions as to necessary factors in experimental design for future research in rheumatoid arthritis and fruitful directions that this research might take conclude the review.

PERSONALITY FACTORS IN RHEUMATOID ARTHRITIS

1. *Personality Traits.*—Certain traits have been noted by various investigators as occurring frequently in people with rheumatoid arthritis. These people are described as leading quiet lives, being "home birds,"[21] as complaining of shyness and social inadequacy,[10] and as having marked feelings of inadequacy

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and inferiority.[32] The majority of some samples[22,26] were noted to be self-sacrificing, overconscientious, and having a strong need to serve others. Also, two investigators[21,26] have commented on the presence of obsessive and compulsive characteristics. Finally, there is some question about a tendency to depression. This has been noted in arthritic children and in their mothers,[7] and in one study of adults[50] a depression preceded the arthritis in 9 of 31 cases.

2. *Personality Problems and Conflicts.*—Among the personality problems reported to be present in arthritis, the most prominent is in the area of *aggression.* Both children[7] and adults[32] have been described as having a strong reservoir of hostility below consciousness, primitive in nature, with sadistic and destructive fantasies. However, the arthritic is tremendously fearful of his angers and resentments,[10] fearful that expression of these feelings will have drastic consequences for him. This may be the reason for his marked emotional self-restriction, especially in the inability to show anger overtly.[7,21,26,32,36] This is especially true in the face of frustration.

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It is not surprising in view of this emotional limitation that there should be a *difficulty in forming close relationships with other people.* In one study[8] half of the 43 patients studied stated that they had difficulty in making friends. Other investigators[1,32,36] also noted this difficulty in developing satisfying relationships with others. The arthritics were described as extremely sensitive and highly perceptive of other's feelings, especially if these were of a hostile or unfriendly nature, allowing themselves to be imposed upon rather than to risk offending and so losing the regard of others. This problem also appeared in arthritic children[7] in that they could not transfer feelings for parents to hospital personnel and could not balance off the frightening aspects of hospitalization with positive feelings of trust and support from hospital personnel.

This difficulty in forming relationships may be related to another problem which could be characterized as *difficulty in achieving separateness from certain key people in the environment.* The arthritic typically has a fear of separation, and, when it does occur, especially from a key figure on whom he depends, there is an inadequate expression of grief, as if to deny that the separation had taken place.[32] It is suggested that this difficulty begins in childhood with an extreme mother-child interdependence and a good deal of conflict in the child about trying to move apart from the mother.[7]

A final personality conflict appears to be in the area of *sexual identification and adjustment.* A number of investigators[1,8,26,50] have reported that the sexual adjustment of their patients was unsatisfactory. In one of these studies,[26] this was spelled out in more detail as far as the female is concerned. The investigators affirmed that there was a rejection of the female role with classical examples of masculine protest reaction in all 29 cases. This resulted in hostile masculine identification. In a few cases the masculine protest reaction was intensified as a defense against fear of sexual attack. Another study[36] showed that in twelve male patients the sexual identification was masculine in only one case, all showing partial impotence. Of ten female patients there was clear-cut masculine identification in nine cases.

Another factor in the problem of sexual adjustment is that two studies[10,31] have reported a high incidence of voyeuristic and exhibitionistic fanatasies among arthritics. This is undoubtedly related to difficulties in sexual identification.

3. *Defensive Techniques.*—The literature indicates that a prominent feature among people who later develop rheumatoid arthritis is a great deal of *muscular activity in sports or hard work.* It has been noted[1,32] that these patients were frequently inclined to be overactive and tended to overwork, to take jobs requiring hard work rather than initiative or responsibility. Female patients[26] had a tendency toward bodily activity, especially outdoor and competitive sports. This was true also in male patients,[36] where 10 of the 12 studied engaged in hard labor or vigorous sports. In one study[10] rheumatoid arthritis patients were compared with low-back-pain patients. The former reported a significantly higher interest in hunting and fishing, and participation in sports. They also had a higher interest in household duties and cooking. Finally, it has been suggested[8] that physical activity gives some form of libidinous satisfaction to these people, except that their drive to be active is in excess of their capacity to find useful channels for the release of their energy. This interest and participation in muscular activity can be thought of as a form of sublimation, or a means of relieving tension, perhaps tension due to unexpressed aggression, with the individual more susceptible to arthritis when the sublimation is no longer available or effective. This is discussed more fully under "Mechanisms."

Another defensive technique is to *stay out of situations that might bring them into disagreement with other people.* This seems to be indicated in male patients[1,8,36] by an absence of competitive employment, little drive to accomplishment, and a lack of wholehearted interest in work. The literature does not indicate ways in which this defense might be exemplified in women.

4. *Evaluation of Personality Factors.*—The material reported in this section is largely descriptive. This is most important in the understanding and treatment of any disorder; but description is crucial only in so far as it enables the investigator or therapist to distinguish the disorder from other disorders. Adequate description, therefore, depends on the presence of control studies or groups. In most of the studies mentioned in this section controls were singularly lacking. A good example of the difficulty thus imposed can be seen in the factor of excessive interest in sports and muscular activity. Only one study here[10] had a control group, and this group was composed of patients with low-back pain. Certainly it is possible that such patients might represent a deviant group in the direction of little interest in muscular activity, leaving the rheumatoid arthritis group more near the general norm. There is no information about the interest and participation of normals in muscular activity and sports against which to judge that of the arthritics. In fact, knowledge of cultural pressures would suggest that there is considerable emphasis on sports for all young people, especially young men. Furthermore, the studies to date have not provided any information about the *meaning* of muscular activity to these people.

Much of the material in this section presents a difficult measurement problem. The conclusions about the presence of intense hostile aggressive feelings below the level of consciousness depend on clinical insights, usually as the result of many psychotherapeutic sessions. Evidence may come from many different places and have to be painstakingly pieced together. However, if indeed this is a common characteristic of rheumatoid arthritis patients, there should be further evidence in the presence of similar patterns on projective tests, like the Rorschach and Thematic Apperception Test. This again necessitates the use of control groups and as yet no studies of this kind have been reported.

The question of sexual identification appears to be an important one, although it is not clear whether difficulties in sexual identification are peculiar to the rheumatoid arthritis patient or are characteristic of a larger group composed of all individuals who are susceptible to stress. It is unfortunate that an adequate device does not exist for measuring objectively the direction and degree of sexual identification, as well as the amount of conscious acceptance of one's sexual role. The lack of such an instrument makes it difficult to evaluate the data obtained by different investigators in this area.

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PSYCHOSOCIAL BACKGROUND FACTORS IN RHEUMATOID ARTHRITIS

It has been reported[1,21] that arthritic patients frequently perceived one or both of their *parents as rather strict and uncompromising in discipline.* More specifically, this has been related in other studies to the role that the mother exemplified. A report based primarily on female cases[26] stated that in the family background there was usually a strong, domineering, demanding mother, and a gentle, compliant father. A different study, based on male patients,[10] said that the mother was perceived as a hard-working, efficient, "Christian" woman, exemplifying self-sacrifice to the point of martyrdom, but also acting as the main disciplinarian, and a strict one at that. Father was seen as inconsistent in his behavior, being both weak and strong, and somewhat unpredictable, as in outbursts of feeling to situations where he usually showed minimal feeling.

A fairly consistent finding has been that the histories of rheumatoid arthritis patients show *the loss of a parent or important relative by some means;* death, separation, or psychologic absence through illness. This loss usually occurred in childhood, or at least by the time of adolesence, and was true for about 50 per cent of the cases.[1,8,31] This factor was also noted in three other investigations[7,10,32] although the percentage of cases in which this occurred was not given.

Two other reports are pertinent in this area. First, it was observed[32] that mothers of rheumatoid arthritis patients seem to have provided an *inadequate feeling of security in early life.* This was manifested by a rejection of the child, either openly, or by an extreme degree of overprotectiveness and overanxiety. The result was a hampering of the child's development toward a free, independent existence, and the fostering of attitudes of dependence and helplessness. Second, in the study of arthritic children[7] it was noted that there frequently was a history of *severe emotional or physical deprivation early in life.*

Evaluation of Psychosocial Background Factors.—Although the data in this section have not been highlighted in the literature, they are particularly intriguing to this author in view of previous research in which he has participated.[15,28] In this previous work normal subjects were studied in laboratory stress situations. It was found that subjects who perceived their mothers as stern disciplinarians and their fathers as rather ineffectual in this area showed a more emergency type of reaction (physiologically and emotionally) than did subjects who perceived father as occupying the strong authority role. The interpretation made was that the former group of subjects would be more susceptible to stress. If this finding is confirmed in further investigations, it would indicate that the material reported in the rheumatoid arthritis studies represents a general condition in people who are susceptible to stress rather than something peculiar to people with rheumatoid arthritis.

Essentially the same result occurred with the loss of a parent by some means. Subjects who had gone through this experience showed a more emergency kind of reaction (physiologically and emotionally) than those who had not lost a parent. Again this may be a factor which in some way makes a person more susceptible to stress.

The last two points in this section, the inadequate feeling of security early in life, and severe emotional or physical deprivation, may well be of the same order as the above.

Clearly, the emphasis here must be of two kinds, accurate and objective measurement and information from a wide source of subjects. Funkenstein and King[15] have suggested a way of measuring the first factor, perception of parental roles in authority, affection, and identification. The second, loss of a parent or significant person, must depend on the subjective report of the subject or others. The third, adequacy of security feelings, still depends on the subjective judgment of the psychiatrist or psychologist and there is at present no other way of obtaining information here. The fourth, early emotional or physical deprivation, must depend on subjective reports of parents or close relatives. The importance of these factors for stress illnesses and particularly for rheumatoid arthritis, however, depends on future information as to the distribution of these factors in the general population.

PRECIPITATING FACTORS

Emotional reactions to disturbing environmental events have been considered by a number of different people to bear some relationship to the onset or exacerbation of rheumatoid arthritis. *Worry over financial matters* has been suggested[9,12,42,43] as occurring frequently in association with onset or exacerbation. Another factor is anxiety over sick relatives or *family worry.*[3,9,12,14,42] *Grief* has often been noted,[3,12,43] which is a part of the general problem of *loss or separation.*[32] *Unrelieved anger* is also suggested as an emotional reaction[26,43] especially if there is an unconscious resentment against men which for some reason is increased.[26]

Perhaps it is pertinent at this point to mention that one author[16] contended that the degree of emotional stability and the satisfactoriness of one's philosophy of life is related to recovery and freedom from relapse of the disease.

There is, however, some disagreement in this area of precipitating factors. One investigator who has seen many arthritic patients[3] has stated that in his experience emotional crisis have seldom been related temporally to the onset of rheumatoid arthritis. In studying 100 soldiers he found an emotional upset to be a possible factor in only one case.

Other negative evidence is from a study for the Empire Rheumatism Council.[30] Here there was a relatively large number of cases, using controls matched with the rheumatoid arthritis patients on the basis of age, sex, and marital status. Both patients and controls were given an extensive questionnaire in which information was obtained about recent traumatic events. This section of the report concludes:

> "The analysis suggests that such mental stresses as may be engendered by the circumstances studied are likely to occur as frequently among non-sufferers as sufferers. From this it follows that any difference between the reaction of sufferers and non-sufferers to these stresses resides in some feature of the sufferer himself rather than in any difference of stress experience. Whatever case-studies or other detailed investigations may show, no evidence was obtained from the present enquiry that traumata or other events likely to be associated with mental stress were precipitating factors in rheumatoid arthritis."

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Evaluation of Precipitating Factors.—Only two of the papers considered in this section have utilized controls, Cobb, Bauer, and Whiting[12] and Lewis-Faning,[30] and only one, Lewis-Faning, had a large sample. The former study had certain definite advantages in design in that it involved a recording of chronological events, both illness and environmental events, over an extended period of years. The latter study was limited to time of onset, asking the respondents about events in the three months prior to onset, and in the two-year period prior to onset. However, each patient was matched with a control and each pair was questioned about events over the same time span. Lewis-Faning concluded that the patients did not report a significantly greater number of traumatic events than the controls, whereas Cobb indicated that the rheumatoid arthritis patients experienced more stressful events than the varicose ulcer patients, although he did note that this was more frequent in the older age group.

It is difficult to compare these two studies and to evaluate their somewhat different results because the methodology is so different. Certainly it is obvious that although Lewis-Faning noted that the arthritics did not report a greater number of traumatic events than the controls, this does not say that the traumatic events were not associated with onset. Furthermore the design that was utilized by Cobb enables a number of observations on the same patient over a period of years, with the possibility of patterns of stress-response relationships arising. These might not be seen if observation was confined merely to a period prior to onset.

A further point might be raised about the Lewis-Faning study. About two thirds of his control group were hospital cases, admitted for the repair of hernia,

or burns, wounds, or fractures. It is thus possible that a sizable number of "accident-prone" individuals were included.

In the other study cited[3] as a source of negative information, the author ruled out the possibility of emotional factors entirely. However, he seems to have overlooked a most important fact. All of the patients used as the source of data for his paper were soldiers in wartime. It seems quite possible that many of these men may have been in conflict about being soldiers, especially as many of them probably came into the Army via the draft rather than as volunteers. Such a conflict might well have had serious physiologic repercussions.

The relationship of stressful environmental events to onset or exacerbation of arthritic symptoms is far from clear, especially as so few well-designed studies have been carried out on the problem. Only continuing, controlled studies can provide the answer.

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MECHANISMS

One of the most important aspects of the relationship of psychologic and social factors with rheumatoid arthritis is that of the mechanisms by which emotions or interpretation of environmental events are related to the physiologic changes of the disease. This is also the aspect about which we have the least amount of information. The material presented in this section is perhaps still so general that it does not really constitute a contribution toward an understanding of mechanisms. However, it represents a tendency in this direction.

1. *Muscle Tension.*—It has been noted[16] how the autonomic nervous system can affect the tone of plain muscles, and how derangement of bodily function can be brought about by the modification of postural tone and activity of the skeletal musculature. The implication here is that in some cases emotional factors can end in bodily derangement and rheumatoid arthritis symptoms. The view has also been expressed[26] that muscle spasms and increased muscle tonus, these being due to emotional conflict, could under certain conditions precipitate an arthritic attack. This has been stated in another way[27]:

> "Many persons with or without clinically obvious arthritic deformities exteriorize habitually their psychic tensions through sustained regional or generalized hypertonia of somatic muscle, which may in turn give rise to musculoskeletal symptoms. These psychogenically induced symptoms can be exceedingly severe. Some patients obtain relief from symptoms when they can be taught not to exteriorize mental tensions through sustained hypertonia of somatic muscle, or when their mental tensions are lessened through directed psychotherapy or through changes in the environment."

There is only one study that has sought to measure the relationship between muscle tension and emotional conflict in rheumatoid arthritis patients.[18] The authors reported that the rheumatoid arthritis group reflected psychologic tensions and conflicts through variations in the tensions of the somatic muscular system. They also found that a hypertensive group reacted in the same manner.

2. *Symbolic Manifestation.*—It has been suggested by a number of authors that the symptoms of rheumatoid arthritis may in some manner be a symbolic manifestation of conflict. For example, the localization of the disease seemed to one investigator to be in the joint or joints in which the conflict was focused.[8] The joint might thus play an important part in an activity that was disliked, or be essential to the assumption of an attitude which expressed in a symbolic way the patient's general demeanor (being "stiff-necked" in attitude toward things), or the joint may have been subjected to a physical trauma which had marked psychologic significance.

This has been discussed further[20,23] in showing how a symptom may be attached to a part of the body through symbolism. For example, we think of a proud, upright person as an individual who stands straight, and an individual with a bent back may be saying, "My pride has been hurt, I can't stand up straight." The same author feels that there is a basis in folklore and etymology for the left side in the collective unconscious to be associated with ideas relating to disaster or misfortune. This may be a factor in patients with peripheral involvement of only the left side.

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At this point it is pertinent to refer to two papers[2,45] dealing with rheumatoid arthritis in soldiers during the last war. The first one describes a number of cases in an Army hospital in this country and notes that in the cases with peripheral joint complaints, 70 per cent had symptoms confined to the lower extremities, in contrast to the percentage encountered in civilian life. The second is concerned with soldiers in the Mediterranean area, where only 19 per cent of the cases with peripheral complaints had symptoms confined to the lower extremities.

The author of the first paper, Boland, is not able to explain the high percentage unless, as he says, "the preponderant use of the lower extremities in soldiers serves as a factor." It is worth raising the question whether or not these men may have had an intense conflict about becoming soldiers. If this were true, the logical place for the symbolic focus of such a conflict would be in the lower extremities. Those soldiers who had a serious conflict about being in the Army, so serious that they were incapacitated because of it, would likely be weeded out before going overseas. For the men in the Mediterranean theater the main conflict might then be one around the meaning of overseas service, that is, getting killed or not. Such a conflict would not necessarily find expression in the lower extremities, but all over the body, as indeed 75 per cent of the cases showed both lower and upper extremity involvement.

3. *Symbolic Control.*—It has been suggested by some investigators that the arthritic symptoms represent a means of controlling or preventing the expression of hostile aggressive impulses, that if the joints are stiff and rigid, motion is limited, the anger will be encapsulated, and danger to others and the patient will be averted. This was expressed some years ago in the following statement[25]:

> "Clinical experience has seemed to indicate to the authors of this book how the fundamental affective trends finding symbolic expression, at the psychological level, in terms of the unconscious

> criminal endeavoring to escape from the reality of his desires, have tied up the joints of various individuals in incapacitating arthritic involvements."

The conclusion has also been drawn from projective tests on arthritic patients that the outer rigidity of the body represents a way of inhibiting something bad within, the bad being unacceptable hostile aggressive feelings.[10]

Closely related to this are some data from a study of the emotional reactions of rheumatoid arthritis patients to ACTH.[36] The authors asked their patients whether or not they remembered their dreams and found that this was associated significantly with improvement or nonimprovement on ACTH. Of twelve patients who reported that before treatment they remembered their dreams, ten had a remission or major improvement. Of nine patients who reported that they did not remember their dreams, none had a remission or major improvement.

Many psychologists feel that remembrance or nonremembrance of dreams is related to leniency or severity of emotional control by the ego, especially of unconscious material. Certainly if this is true there is a continuum here, and patients who did not remember their dreams had relatively more repression than did patients who remembered them. They also had more intractable rheumatoid arthritis in that it did not yield to ACTH therapy.

4. *Evaluation of Mechanisms.*—It is obvious that there are some large gaps between activity of the skeletal musculature and the symptoms of rheumatoid arthritis. Furthermore, there is no evidence in the literature that people predisposed to arthritis are any different from other groups in terms of muscle tension. The only study that attempted some measurements in this area[18] found that the arthritics were no different from hypertensives in reflecting psychologic conflict by muscle tension. Clearly it would seem that this is one of the weakest areas of our present knowledge about rheumatoid arthritis. Until adequate measurements of muscle tension of rheumatoid arthritis and other groups are made, and until we understand the physiologic effects of sustained muscle tension, this aspect of the problem is questionable.

Symbolic manifestation is close to the area of conversion symptoms, and conversion symptoms as they have traditionally been defined do not produce the drastic physiologic changes seen in rheumatoid arthritis. However, a number of writers have felt that certain arthritics have features which are suggestive of conversion symptoms. If there is to be clarification in this matter, a needed first step will be a careful study of the site of symptoms and the relation of this to relevant psychodynamic factors. The literature to date is only suggestive that such a relationship may exist.

In talking about symbolic control we see the biggest gap between the psyche and the somatic symptom. There are many intermediate steps here that we cannot yet formulate or even find a logical basis for speculation about. However, the empirical evidence presented in the McLaughlin study[36] is arresting. Seldom in the field of psychosomatic medicine does one find such a strong relationship between psyche and soma as these investigators found between dream

remembrance and reaction to ACTH therapy. Furthermore, if one assumes a relationship between remembering dreams and strictness-leniency of ego control, these data fit with the conclusions of other investigators. The typical rheumatoid arthritis patient is said to be an individual who controls his emotions tightly and does not form close emotional relationships with other people. It may be that in some cases there is a positive relationship between amount of emotional control and susceptibility to rheumatoid arthritis and, further, between strict control and severity of rheumatoid arthritis. Certainly the empirical evidence in this one study merits further investigation. One necessary step will be to enlarge and scale the questions about dream remembrance in terms of frequency, duration, and vividness, also to search for other methods of obtaining objective measures of ego control. The long and exhaustive techniques of the clinical psychologist or the extensive interviews of the psychiatrist do not lend themselves to studies in which a large number of cases is under consideration. These scaled questions will then need to be administered to subjects in which there is a careful medical history in terms of diagnosis, severity, and course of disease. Associations can then be sought between frequency, duration, and vividness of dreams and the type and course of the disease process.

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RHEUMATOID ARTHRITIS AND SCHIZOPHRENIA

The relationship between rheumatoid arthritis and schizophrenia appears from the literature to be one in which there are certain similarities in personality. Also there is some evidence indicating that it is unusual for the two diseases to be present simultaneously in the same individual.

The similarity was noted twenty years ago,[38] the only difference being the outlet thrust upon the individual. As Nissen wrote:

> "In one, dysfunction of the personality predominates; in the other dysfunction of the bone and joint furnishes an unrecognized alibi for withdrawal from active life, or a means, through capitalizing disability, of gaining attention which had been previously unobtainable."

In a study of equal groups of atropic and hypertrophic arthritics,[14] the premorbid personality was classified as being predominantly schizoid, syntonic, or mixed. Twice as many of the atrophic cases showed predominately schizoid features as did the hypertrophic cases, whereas this situation was reversed when the syntonic features were considered.

Rorschach studies on male arthritics[10] showed many of the pathologic features usually seen in the psychotic personality, including contamination and confabulatory responses, color naming, and extensive poor form level. Thirteen of the 25 cases studied were this seriously disturbed.

The unlikelihood of the simultaneous occurrence of the two disorders was noted in a study of a mental hospital[39] where there was not one arthritic among 2,200 patients. Also in 500 arthritic cases, there were only 3 cases of mental disease, and in these 3 gonorrhea had been responsible for the arthritis.

In a study of hospitalized psychotics in Massachusetts in 1938,[19] it was found that only 20 of 15,196 cases were partially or completely bedridden with arthritis. This was 17 times less than the rate in the nonpsychotic population. In addition, the results of 3,000 autopsies of psychotics showed no frank arthritic joints.

Further evidence here comes from a case presentation of a woman with rheumatoid arthritis who became psychotic.[21] During the four years she spent in a mental hospital the rheumatoid arthritis was quiescent, but upon recovery from the psychosis the arthritis returned to the extent that she became completely crippled. A somewhat similar case[34] showed evidence of a psychotic break, followed later by an exacerbation of arthritic symptoms.

1. *Evaluation of Relationship of Arthritis and Schizophrenia.*—In the two main studies reported in this section, that by Nissen and Spencer[39] and that by by Gregg[19], there are certain serious difficulties. In the study by Nissen and Spencer there is the difficulty of accurate determination of arthritic symptoms in a large psychotic population. This depends partly on the acuity of the physician in recognizing true arthritic conditions and partly on the screening process used for finding the group of patients that have some sort of rheumatic complaints. If one depends on disabling conditions, it must be on the assumption that both psychotics and nonpsychotics react in the same manner to bodily conditions. This is a dangerous assumption. Furthermore, Nissen and Spencer do not state the factors they would consider in making a diagnosis of rheumatoid arthritis in psychotics.

The study by Gregg is confusing in comparing bedridden and disabled patients and in not distinguishing between rheumatoid arthritis and other forms of arthritis or chronic rheumatism. In this case the question of diagnosis is even more acute than in the other study. Also it must be noted that there are few good studies of the distribution of rheumatoid arthritis in the general population.

Although many workers in this field think that rheumatoid arthritis and schizophrenia have much in common, the evidence thus far must be considered mainly suggestive. The suggestiveness is sufficiently strong, however, for undertaking further careful, objective research.

DISCUSSION

The evidence from the literature indicates that we still do not have a clear picture of the role that psychologic and social factors play in predisposition, onset, or exacerbation in rheumatoid arthritis. It does indicate, however, that these factors have a role in some cases of rheumatoid arthritis and that the importance of this role varies from one individual to another. It is clear that psychologic and social factors can be considered as only part of a series of factors, all of which contribute in some measure to the disease. An accurate determination of the relative importance of each of the factors in this series for a given individual must wait until we have better objective measuring devices and mathematical techniques for weighting the results of these. In the meantime, well-designed studies can contribute much toward the assessment of the im-

portance of emotions, conflicts, family and group pressures, and other psychosocial variables in arthritis.

1. *General Factors in Research Design.*—As pointed out in the evaluation sections, one of the crucial problems in new research is that of control groups. Studies to date in this area have shown a paucity of controls. The crucial question is whether or not people with psychosomatic disorders have many psychosocial factors in common, or whether there is a higher incidence of these in certain diseases. A casual survey of the psychosomatic literature highlights the commonality rather than the specificity. The use of control groups, normals as well as other disease groups, will help decide what factors contribute to a general susceptibility to stress and what to the predisposition to a specific disorder.

Another crucial aspect of future studies lies in the necessity of correlating the results of a careful medical examination with the occurrence and strength of various psychosocial data. It is important to group the rheumatoid arthritis cases according to type (peripheral, spondylitic, etc.), severity, duration, frequency of exacerbations and remissions, age of onset, etc. This necessitates the use of larger samples, which is expensive and time consuming, but it would seem that previous studies have been weak because of neglect here.

A third point has already received attention, that being the necessity of using objective measuring instruments wherever possible. This is possible in many of the areas discussed in this paper. The behavioral sciences now have at their disposal a variety of ready techniques or knowledge about the construction of techniques for this. In particular this is true for scaling techniques in attitudes and practices. It is possible to devise questions that, when added together, give information that do not reveal to the subject the investigator's purpose. It must be recognized, however, that some material, especially that pertaining to individual psychodynamics, cannot be handled in this manner. In these cases it is important to present as far as possible the evidence for conclusions drawn.

A fourth general point is relative to longitudinal studies. Ideally such a study might begin with a group of subjects who have not yet developed rheumatoid arthritis. Such a group might be chosen from people who report that they have morning stiffness. Cobb[11] has suggested, for example, that morning stiffness may exist in all rheumatoid arthritics before definite symptoms of the disease appear, but that all people with morning stiffness do not develop rheumatoid arthritis. Therefore, some of these subjects would be expected to develop rheumatoid arthritis, others not, and psychosocial data obtained during the premorbid state could then be considered for each group. The temporal relationship between environmental events and the course of the disease would then come under scrutiny, especially as some of the subjects would not develop rheumatoid arthritis. Though there are difficulties of personnel commitment and financing, there is much merit in a research design which includes this feature.

2. *Specific Areas of Fruitful Study Based on Previous Work.*—A number of specific topics would seem to hold promise for advancing our knowledge about

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rheumatoid arthritis. First, there is the variable of the importance of losses or separations in the lives of arthritics, beginning in early childhood. Which parent was lost? What happened in the family when the mother was lost? What were the reasons for losing father? Were there any common factors in terms of type of death or loss? What kinds of loss were there besides death? In later life it would be fruitful to ask what kinds of situations are felt to be losses or spearations and, thus, perhaps, activators of a basic separation anxiety.

Second, is the factor of activity patterns. This involves a determination of pressures toward activity in different subcultural groups, types and amount of activity patterns in these groups. With this background, the relative degree of activity, holding class or subcultural factors constant, in arthritics and nonarthritics can be determined. Inasmuch as heightened bodily activity "makes sense" in terms of a psychologic defense against strong aggressive drives, it is important to answer this question for rheumatoid arthritis.

Third, is the question of remembrance or nonremembrance of dreams. As suggested previously, this may have some relevance for the amount of ego control. The frequency, duration, and vividness of recall need to be studied and scaled and information obtained from other disease groups as well as from subjects free from disease.

Fourth, is the variable of direction and acceptance of sexual identification. Evidence from the literature is sufficiently strong here to hypothesize that sexual identification will be reversed. There is no evidence about the acceptance or rejection of such identification. Important here will be the presentation of material that forms the basis of the investigator's judgment as to sexual identification.

Fifth, is the problem of the perception of parental roles in authority. Again there seems sufficient evidence in the literature to hypothesize that the mother will be perceived as dominant here. In addition, it is important to obtain information about the perception of parental roles in affection and identification. Considering three factors here makes possible a number of combinations, thus providing more specific information than could be obtained from asking about authority alone. Also it is important, wherever possible, to get some judgment by the investigator, and the parents themselves, as to the manner in which they fulfill these roles, or think they fulfill them.

Finally, the symbolization of symptoms merits further attention. Supporting evidence here is not so strong, and unfortunately we do not yet have the tools for a conclusive experiment in this area. Furthermore, this may be a factor in only a small number of cases. However, this factor should be considered wherever possible in a research design.

3. *New Areas of Study.*—Certain aspects of the concept of self may prove to be fruitful in new research. A consideration of the personality characteristics and problems of the arthritic indicates that the way he sees himself in relation to the rest of the world may be important to his disease. Two aspects of the concept of self would seem to be important. First there is the way he sees his body in fantasy, or his body image. If there is truth to the assertion that arthritic symptoms represent a control of disturbing aggressive impulses, one would

expect the body image of these people to be different from nonarthritics. In fact, this would seem to be one way to test the hypothesis of symbolization. Second, there is the way the individual sees himself in terms of personality characteristics. The study by Funkenstein and King, mentioned earlier, indicated an association between ability or inability to master continued acute stress and this aspect of self concept. Subjects who showed a discrepancy between self rating and the way they thought others would rate them on a series of traits did not handle continued acute stress as well as subjects where there was little or no discrepancy. This relationship was strong enough to indicate its possible importance in studying stress diseases.

Second, social scientists now posit that social mobility factors are important sources of threats to and tensions within the individual. This is especially true if this mobility is not encouraged by the individual's family, or if it precipitates conflicts over values. Important variables here are the distance the individual moves in the class scale, the changes he makes in class identification through marriage, organizations, attitudes, etc., and the support from wife and other class members for his new values. Also of great importance are class pressures toward the control of emotional expression and legitimate avenues for such expression, especially if these are at variance with outlets in his previous class position.

Finally, there are indications that religiosity bears a relationship to susceptibility to stress. Swaim[49] made a frank appeal for the use of spiritual exercises as an adjunct to medical treatment in this disease, believing this would have a beneficial effect on the underlying anxiety and resentment. Funkenstein and King found a significant relationship between religious practice and cardiovascular reaction during laboratory stress, in that those who indicated frequent religious practice had a more homeostatic pattern, while those who indicated weak or infrequent religious practice had an emergency type of pattern. Though this area has tended in general to be ignored in psychologic and medical research, it may well prove to be a fruitful area.

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SUMMARY

The literature on psychologic and social factors associated with rheumatoid arthritis has been reviewed according to personality characteristics and conflicts, social background factors, precipitating factors, mechanisms, and the relationship between rheumatoid arthritis and schizophrenia.

After an evaluation of this material, it is suggested that general factors in research design include control groups, careful medical history and examination, objective measuring devices in the psychologic and social area, and longitudinal studies wherever possible. It is suggested that fruitful areas for further research are the importance of losses and separations in childhood, activity patterns, remembrance of dreams, direction and acceptance of sexual identification, parental roles in authority, and symbolization of symptoms.

Finally it is suggested that new areas of study might include certain aspects of the concept of self, social mobility factors, and religious practices and expressions.

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THE DECLINE AND FALL OF SYPHILIS IN NEW YORK STATE

III. Early Acquired Syphilis

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THIS is the third in a series of papers dealing with the downward trend in reported syphilis in New York State (exclusive of New York City). The previous papers were concerned with the over-all trend in rates,[1] and the trends in rates for early congenital syphilis,[2] since 1936. Our general objective has been to interpret the significance of the downward trend and to identify those aspects of, or factors in, the natural history of syphilis which might be expected to maintain the trend, and to prevent the occurrence of large-scale outbreaks in the future.

The specific objective of this third paper is to examine the evidence we have developed in the previous papers in the light of the age and race specific morbidity rates for early acquired syphilis since 1944.

The major items of evidence brought forward in the previous papers are the following:

I. The occurrence of a major outbreak of syphilis in New York State (exclusive of New York City) between 1942 and 1948 in which the annual incidence of early syphilis reached the highest point since reporting began in 1936.

II. A steady decline in reported late acquired and congenital syphilis in both the white and non-white populations. The total decline was greater in the non-white populations, although the relative decline was approximately the same in both population groups.

III. There was a steady decline (approximately 90 per cent since 1936) in the annual incidence of early congenital syphilis in both the white and non-white population groups which apparently reached a plateau in 1951.

IV. A decline in the prevalence of reported syphilis in the adult population in the child-bearing ages amounting to 58 per cent, based on a comparison of birth certificates with the syphilis roster in Buffalo, New York, in 1938, and again in 1953.

The evidence summarized above and the previously analyzed data suggest three inferences or conjectures with regard to the control of syphilis. These inferences will be restated and briefly discussed:

A. *Selective Immigration.*—The outbreak of early syphilis, which reached its peak in 1946, occurred during a time when syphilis control services in the State had been well established for ten years. Some dislocations and deficiencies existed because of wartime conditions. The outbreak was accompanied by a selective type of natural population increase and immigration during the decade 1940-1950 which resulted in a 50 per cent increase in the non-white population and a 15 per cent increase in the white population. Because of the higher rates in the Negro and because of the tendency for immigrants to be of younger ages, it was suggested[1] that the outbreak may have reflected selective immigration rather than increased transmission within the State.

B. *Effectiveness of Control Procedures.*—The outbreak reached the highest annual incidence on record, in spite of the fact that syphilis control services were well established and even intensified during the war years. It was noted[1] that the relative decline in early syphilis was approximately the same in the periods 1936-1937 and 1946-1949. In the earlier period the arsenicals and bismuth were the drugs of choice, whereas penicillin was available in the latter period. It was suggested that we re-evaluate the efficacy of early diagnosis and prompt treatment as being a completely effective measure in the control of outbreaks. The data suggested that the ultimate control of syphilis will require something more than early diagnosis and prompt treatment. As a corollary to this inference, it was suggested that the current attitude of laissez faire toward the epidemiology of syphilis should be changed. If this is done, we can continue to learn much more about the factors which influence the continued transmission of the disease.

C. *The "Steady State".*—While the annual incidence of early syphilis and the discovery rates for late and congenital syphilis have decreased sharply, both have shown a tendency to level off since 1951. This suggested that the annual incidence of early syphilis may be reaching a minimum level. This level may be so high that another outbreak could occur and reach fairly large proportions[2] before effective control procedures could be established.

The general conclusion was that the current optimism with regard to the ultimate control of syphilis is not justified. Continued interest in the epidemiology of syphilis, both from the laboratory and field points of view, is necessary if the downward trend is to be maintained.

In the present paper, these broad inferences are tested with data on the annual incidence of early acquired syphilis. The source of the new data is case reports of early acquired syphilis received from physicians and clinics in Upstate

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New York and filed with the Bureau of Epidemiology and Communicable Disease Control, New York State Department of Health, Albany, New York, since 1944.*

The administrative mechanism of case reporting is described in previous publications in this series and elsewhere.[3] The reporting system has been established since 1936, and, because of the technical assistance given to local health officers and physicians, case reporting is regarded as fairly complete with respect to primary and secondary syphilis. Underreporting may occur because of the clinical difficulty of recognizing "asymptomatic" early syphilis. In Upstate New York, early asymptomatic syphilis is defined as early syphilis, with *none* of the usual presenting signs and symptoms, but with a history of such signs during the past calendar year, or other evidence that infection has taken place during the past calendar year of the patient's life.

Between 1936 and 1953, the proportion of early syphilis cases, classified as early "asymptomatic" syphilis, increased steadily from 19 per cent to 57 per cent. This suggests that physicians and health officers have been increasingly alert to the diagnosis of early syphilis.

TABLE I. REPORTED CASES OF EARLY ACQUIRED SYPHILIS PER 100,000 POPULATION BY AGE AND ETHNIC GROUPING IN NEW YORK STATE (EXCLUSIVE OF NEW YORK CITY), 1944-1953

WHITE

AGE	'44	'45	'46	'47	'48	'49	'50	'51	'52	'53
Age 1–14	0.1	0.5	0.2	0.4	0.4	0.3	0.3	0.0	0.0	0.1
15–24	30.2	43.5	87.7	48.3	24.4	15.8	9.3	4.1	3.6	3.6
25–34	26.5	45.4	83.9	42.9	25.1	13.7	5.9	3.4	3.0	2.9
35–44	15.0	16.6	26.0	18.1	11.0	5.3	3.1	2.3	1.3	0.4
45–54	4.9	6.2	8.8	6.7	4.7	2.5	2.0	0.7	1.0	0.4
55 & over	1.5	1.4	3.4	2.1	1.9	0.9	0.5	0.4	0.4	0.4

NON-WHITE

AGE	'44	'45	'46	'47	'48	'49	'50	'51	'52	'53
Age 1–14	26.9	16.0	28.0	17.9	25.1	2.6	4.8	2.4	2.3	0.0
15–24	1303.0	1722.5	2032.4	1702.4	1015.8	650.6	397.4	241.8	149.1	109.7
25–34	645.9	838.6	1314.2	903.8	692.3	455.8	330.3	208.0	98.7	70.2
35–44	154.1	274.8	296.8	220.5	207.4	180.7	144.3	90.3	57.2	23.4
45–54	62.0	107.4	147.4	65.5	48.2	51.4	62.0	7.8	11.1	10.7
55 & over	30.8	27.5	59.0	25.0	6.0	11.2	31.7	5.8	0.0	0.0

Age and race specific attack rates for early acquired syphilis are shown in Table I and Fig. 1 in single years from 1944 to 1953. Initially, the rates were tabulated by sex, color, and 5-year age groups. Since separation by sex and

*Data were made available to us through the courtesy of Dr. R. F. Korns, Director, and Dr. Robert Albrecht, Acting Director, of the Bureau of Epidemiology and Communicable Disease Control.

5-year groupings did not add significantly to the analysis, the rates were combined and presented in 10-year age groups in the white and non-white* populations.

In general, the age specific rates among the white population follow the same pattern as age specific rates among the non-white population throughout the 10-year period. Between 1944 and 1946 the rates among the white population in age group 15-34 tripled, while the rates among the non-white population doubled. The downward trend was somewhat more abrupt among the white population after 1946. The principal differences from the general pattern are in non-whites in the 25-34 year and 35-44 year age groups. The trend in rates in the 15-24 group among non-whites parallels the white rates closely but at a much higher level.

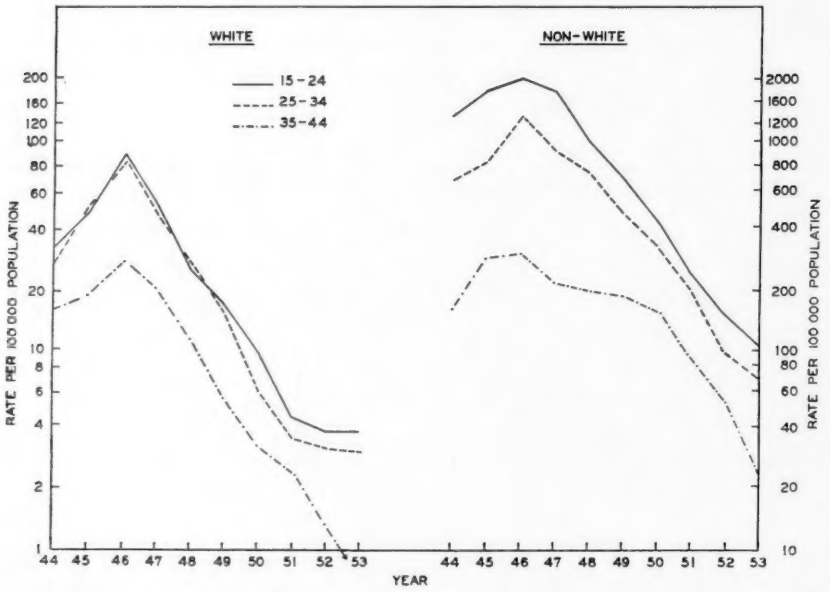

Fig. 1.—Reported cases of early acquired syphilis per 100,000 population by age and ethnic group, New York State (exclusive of New York City), 1944-1953.

Another aspect of the changing risk of acquiring syphilis is shown in Figs. 2 and 3. Fig. 2 is a chart of the median age at onset for whites and non-whites in single years over the 10-year period; Fig. 3 shows the accumulated percentages in each age group for whites and non-whites in the years 1944 and 1951. Both charts show that the age pattern among non-whites is apparently approaching that of the white population.

One final point concerning the trends in age and race specific rates should be noted. The logarithmic scale used in Fig. 1 brings out the percentage or

*According to the 1950 census, the non-white population made up 2.6 per cent of the population of New York State (exclusive of New York City).

proportionate trends in each population group. An arithmetic ordinate would reveal much greater variation in the rates for the non-white population than for the white population. Rates among the non-white population have been at a much higher level throughout the time period. The relative risk among the two groups can be estimated by dividing each cell in Table I for "non-white" by the corresponding rate in the "white" portion of the table. This analysis shows that the risk is 10 to 70 times as great in the Negro population, depending on the age groups which are being compared.

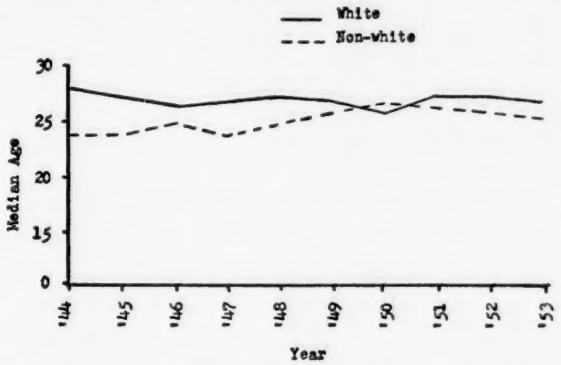

Fig. 2.—Median age of reported cases of early acquired syphilis, and ethnic group, New York State (exclusive of New York City), 1944-1953.

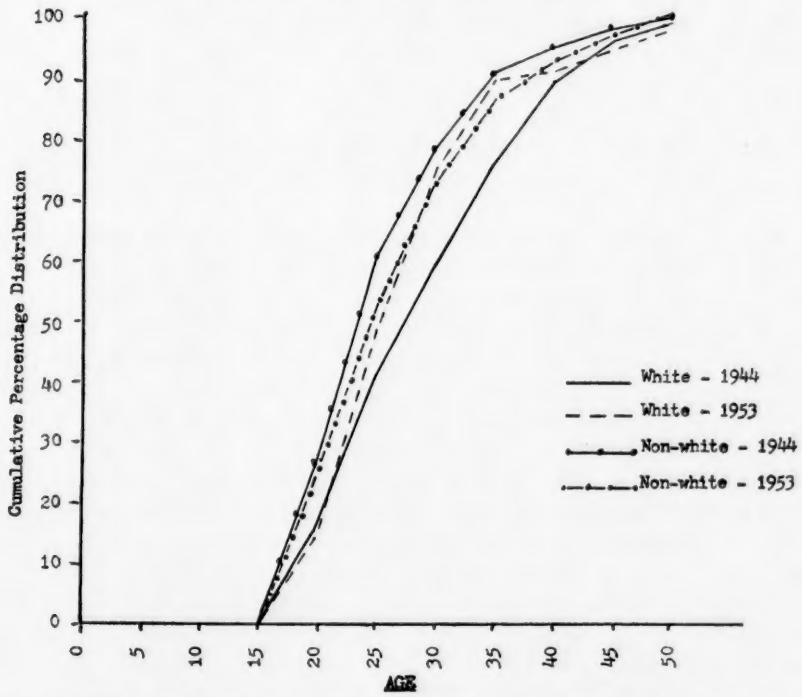

Fig. 3.—Reported cases of early acquired syphilis per 100,000 population cumulative percentage distribution by age and ethnic group, New York State (exclusive of New York City), 1944-1953.

DISCUSSION

The inferences stated at the outset may now be re-examined in the light of the age and race specific morbidity rates presented above.

A. *Selective Immigration.*—The annual incidence of early syphilis tripled between the years 1944 and 1946 among the white population; among the non-white population, the annual incidence doubled. Over the same period of time, the median age at onset among whites decreased slightly, while it increased among the non-white population. Taken together, these two facts suggest that the increase in transmission was relatively much greater among the white population than it was among the non-white. At the same time the relative population increase was of a reverse order; i.e., the non-white population increased relatively much more than did the white population. It seems unlikely that the increase in the non-whites had a major bearing on the over-all increase. The outbreak seems to have been due to an increase in the transmission of the disease rather than a selective immigration of infected individuals. This conclusion is supported by the fact that sex specific rates are approximately equal both in the white populations and the non-white populations.

B. *Failure of Control Procedures.*—The sharp and explosive character of the outbreak between 1944 and 1946 is something which should give serious concern to health administrators. During the period 1942-1946, control procedures were stepped up; rapid treatment facilities were established, first with arsenicals, and later with penicillin. Clinic services were expanded. The State Department of Health through its Division of Syphilis Control, actively promoted the control of syphilis among the local health departments, emphasizing contact investigation. In general, the effort included every useful technique in syphilis control which was available at that time. In spite of these efforts, rates reached the highest recorded level since reporting started. In other words, control procedures apparently did not effectively hamper increased transmission of the disease.

Penicillin was introduced coincidentally with the peak of the outbreak in 1946. When the drug was first introduced, provisions were made for hospitalization of patients so that penicillin could be effectively administered. As the delayed acting antibiotics became available, they were promptly placed in distribution and furnished to physicians and clinics by the State Health Department without charge to the physician. Undoubtedly, the drug improved the treatment of individual patients. At the same time, it is not clear that penicillin, per se, was responsible for termination of the outbreak. It has already been pointed out that the downward trend between 1936 and 1939 is closely parallel to that between 1946 and 1949. Perhaps the coincidence of the introduction of penicillin and the sharp decline in the incidence of syphilis may have given many health officers a false sense of security.

The reason for the failure of control procedures is not clear. There are at least two broad possibilities. The first is that it is frequently impossible to bring people with lesions under treatment before they successfully transmit the disease to sexual partners. The second is that effective transmission may occur more frequently than we realize in the absence of significant lesions.

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C. *The "Steady State".*—The sharpness of the 1946 outbreak emphasized the fact that under the proper conditions, which we do not completely understand at the moment, the transmission of syphilis can go on at a very rapid rate. During the last several years, the number of early cases reported has been approximately 200 per year. Thus, simply by repeating the 1944-1946 experience, the annual number of early cases might increase to 600. Since it takes some time to mobilize personnel and to revise programs, it is obvious that the target for the "minimum level" should be much lower than it is at present.

CONCLUSIONS

The data presented in this paper have been analyzed in terms of the three inferences stated at the outset: selective immigration, effectiveness of control procedures, and the "steady state." Evidence adduced from this study of the age and race specific attack rates for early acquired syphilis in New York State (exclusive of New York City) during the period 1944-1953 suggests that there was a sharp increase in transmission of the disease in the white and non-white populations. Therefore, it seems reasonable to reject the inference that population movement, in terms of the large scale immigration of highly infected population groups, played a major role in the outbreak. Undoubtedly, the rapid mobility of the population during the war and during demobilization favored the transmission of syphilis in many ways which we cannot measure. At the same time these forces, whatever they are, seem to have had approximately the same effect on the white and non-white populations with regard to the transmission of syphilis.

As to the effectiveness of control procedures, the evidence presented suggests that they were not effective in control of the wartime outbreak. One can and should temper this conclusion somewhat by offering the opinion they were undoubtedly more effective than no control procedures at all. The fact is that a major outbreak occurred in spite of them. The most conservative view one could take of the situation is that early diagnosis and prompt treatment are not nearly as effective in the control of the syphilis outbreak as it is in the treatment of the syphilis patient.

The validity of the inference regarding the "steady state" cannot be tested with the data presented in this paper. It was suggested because of the tendency for the rates for early congenital syphilis to become stationary, as previously reported in this series.[2] A few suggestions in the present data support such an inference. For example, rates for early syphilis among the white population in the 15-24 year and 25-34 year age groups have remained nearly constant since 1951 while the rates in the same age groups among the non-white population steadily declined.

On the basis of the New York State experience, it is apparent that the ultimate control of syphilis is far from an accomplished fact. In particular, attention to two aspects of the current situation might be expected to produce significant results in terms of a continued downward trend.

1. Systematic efforts to locate the population groups most at risk of acquiring the disease are needed. This might be done by means of relatively simple epidemiologic studies of reported cases. For example, the data in this paper is for all of Upstate New York. A tabulation of the cases and rates by place of residence and race revealed wide variation and clearly pointed out the geographic areas where the risk remains high. More intensive epidemiologic studies of such groups isolated in this way would reveal which host or environmental factors are still hampering the control of syphilis.

2. The studies suggested above should be accompanied by intensified control procedures in these areas, and among the particular subgroups isolated. Such procedures would include contact investigation and health education programs especially adapted to the particular groups at greater risk, as well as the removal of any barrier to the prompt medical treatment of infectious cases.

This type of effort should be effective in further reducing the incidence of early syphilis; at the same time, it might well reveal how early diagnosis and prompt treatment can be made an effective control measure.

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Review

THE OSLO STUDY OF THE NATURAL HISTORY OF UNTREATED SYPHILIS

An Epidemiologic Investigation Based on a Restudy of the Boeck-Bruusgaard Material

A Review and Appraisal

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INTRODUCTION

GJESTLAND has recently completed in monographic form[1] a retrospective follow-up study of Boeck's famous collection of untreated syphilitics. This recent investigation is an outstanding example of the application of modern epidemiologic methods[2,3] to the natural history of chronic disease. It is, moreover, a convincing illustration of international cooperation in the field of medical science. This cooperation has included two national departments of health (United States Public Health Service and the Norwegian Public Health Service); three universities (the Universities of Oslo and Bergen in Norway and Columbia University in New York); and a number of physicians and statisticians on both sides of the Atlantic.

The basis for the present investigation is the well-known Boeck material, first described in 1929 by Boeck's successor, E. Bruusgaard.[4] It has now been re-studied in the department of Bruusgaard's successor, Niels Danbolt. Forty to sixty years ago (1890-1910), Boeck, then Professor of Venereology and Dermatology, hospitalized approximately 2,000 patients with primary and secondary syphilis until the lesions healed without specific treatment. These lesions were carefully described on admission to the hospital and their regression and time of disappearance noted in well-kept records. Bruusgaard, in 1925, began a follow-up of these patients in order to show "how syphilis progresses when little or no treatment is given and the patient's defense mechanism is allowed to combat the disease alone."[4] His study led to the famous and internationally quoted "Bruusgaard material," which has formed the basis for prognostic statements concerning both treated and untreated syphilis for more than 25 years. Gjestland's carefully planned and executed epidemiologic re-study of this unique

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clinical material has been presented as a dissertation to the University of Oslo. The results should be of interest to epidemiologists and to the large group of physicians concerned with the natural course of syphilis in particular and of chronic disease in general.

The re-study, supported by the Research Grants Division of the National Institutes of Health, United States Public Health Service, owes its origin to the continued interest in Bruusgaard's work by many persons, particularly Moore of Johns Hopkins University, and those associated with him as staff and students. The actual investigation came as a result of discussions both here and abroad among Moore, Danbolt, Guthe (now of WHO, then a postgraduate student at the Johns Hopkins School of Hygiene and Public Health) and Heller, then Chief of the Venereal Disease Division of the United States Public Health Service. Following a visit in 1947 by Moore to Oslo to examine the basic data, funds were made available and the detailed study was undertaken in 1948 by Gjestland, also a graduate of the Johns Hopkins School of Hygiene and Public Health. The facilities of Danbolt's department in Oslo were placed at his disposal. After a period of careful planning and two years of data collection, Gjestland spent the major part of the academic year 1951-1952 as a research associate in epidemiology at the Columbia University School of Public Health, during which time a great part of the analyses were made.

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The objectives of the present paper are: (a) to review and appraise this important contribution; (b) to present some of the details of the planning and execution of the investigation as an excellent example of the epidemiologic method; (c) to provide a brief résumé of the results of the study for the American reader; and (d) to emphasize the significance of this investigation for the natural history of chronic disease.

Arising from basic scientific principles (exact observation, correct interpretation, rational explanation, and scientific construction) and developing as a result of studies of epidemics and of infectious diseases, the epidemiologic approach to the investigation of the natural history of disease is an orderly scientific method of study comprising a continuum of several well-defined steps. Gjestland's study adhered to a plan of five steps: (1) definition of the nature, extent, and significance of the problem and clarification of objectives; (2) appraisal of existing information; (3) formulation of hypotheses; (4) testing of hypotheses; and (5) conclusions and practical application.

I. DEFINITION OF NATURE, EXTENT, AND SIGNIFICANCE OF THE PROBLEM AND CLARIFICATION OF OBJECTIVES

This initial phase began in 1948 with the original suggestions of Moore, Danbolt, Guthe, and others. These suggestions were incorporated by Gjestland into a plan which provided clear definition of the nature, extent, and significance of this problem, a clarification of the objectives, and a proposal of important questions which might be answered by a re-study of this material.

Gjestland introduced the discussion of the nature of the over-all problem with a quotation from Stokes[5]: "No one who has had even a limited experience in answering the questions on which students and physicians seek information in their practical contacts with the disease can fail to realize that the great ailment of modern syphilological practice is a lack of comprehension of the why and wherefore, rather than the what to do." Comprehension of the "why and wherefore" lay in a better understanding of the prognosis of untreated syphilis. The beneficial effects of treatment in modifying the biologic course of syphilis infection is well known. What was lacking was quantitative information on what happens to those who go untreated. The reason for this lack lay in the absence of studies of large groups of untreated patients, thoroughly diagnosed and observed over sufficient periods of time. The Boeck material provided such a large group of patients. Boeck's conviction as to the prognosis of syphilis is summarized by Bruusgaard[4*]: "The immune mechanisms of the body are the most important factors in combating this disease. The specific drugs must be considered as adjuvants only; they are not potent enough to exterminate the disease completely—the antibody formation is disrupted; the course of the disease becomes atypical and serious complications may result. Specific drugs should be used only in cases where the body does not seem able, itself, to overcome the disease—they should then be used in great quantities and over a long period of time. You are at the mercy of the drugs." Thus, mercury was seldom administered in Boeck's department and potassium iodide became the nonspecific drug of choice in all cases where the clinical course indicated its use. This policy of management was firmly established by January, 1891, and was followed in all cases until late 1910, when the first injection of 606 was given. This attitude of Boeck provided approximately 2,000 patients who were untreated for primary and secondary syphilis. These patients were hospitalized until all evidence of primary and secondary syphilis disappeared and received no treatment during this period, with the exception of potassium iodide in some instances. Since other syphilologists in Norway did not share Boeck's opinion as to the efficacy of mercury, it is possible that some of these patients were treated after discharge from the University Hospital. To what extent this was the case could only be clarified by follow-up information. All that could be said at the outset was that this was a group of patients untreated for primary and secondary syphilis, but unknown as to subsequent therapy.

Further significance of the problem of prognosis is emphasized by the reliance of modern syphilologists upon the results of Bruusgaard's investigation of a small sample of Boeck's patients in 1925-1927. Bruusgaard located a total of 473 patients; some he actually examined; on others he recorded information obtained through records of clinic or hospital visits, autopsy records, and death certificates. This gave Bruusgaard information on patients who had had syphilis for intervals ranging from 3 to 40 years. No mention is made as to antisyphilitic treatment during these intervening years. By combining his data on the 309 living and the 164 dead persons on whom there was information from 3 to 40 years after discharge from the hospital, it has been estimated in authoritative works of

*Referring, of course, to the pre-arsenical-bismuth-antibiotic era.

reference that the probable outcomes of untreated syphilis are as shown in Table I. This table suggests that approximately two-thirds of patients with untreated syphilis will experience no disabling effects of the disease.

TABLE I. SUMMARY OF BRUUSGAARD'S DATA AS TO ULTIMATE OUTCOME OF UNTREATED EARLY SYPHILIS

PATIENTS SHOWING AT RE-EXAMINATION OR DEATH	PER CENT OF TOTAL NUMBER (473 PATIENTS)
Neurosyphilis	9.5
Cardiovascular syphilis	12.8
Benign late syphilis	12.2
Latent syphilis (no clinical evidence, blood serologic test positive)	14.1
Spontaneous "cure" (no clinical evidence, blood serologic test negative)	27.9
Died of syphilis other than cardiovascular or central nervous system	0.8
Died of some other cause (cancer, tuberculosis scattering)	22.6

From Moore, J. E.: The Modern Treatment of Syphilis, ed. 2, Baltimore, 1943, Charles C Thomas, p. 40.

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As these estimates of prognosis have passed from textbook to textbook and from one scientific paper to another, they have taken on a significance entirely unwarranted by the nature of Bruusgaard's data. Bruusgaard himself warned that acceptance of his data should be made "with the reservation which the nature of the material makes necessary."[4] Nevertheless, most of the existing hypotheses on the outcome of untreated syphilis are based upon Bruusgaard's study. Critical reviews and appraisals of the Bruusgaard material by Harrison[6-8] and Sowder[9] have shown that Bruusgaard's sample was highly selected, not being representative either of the Boeck material or of untreated syphilis as a whole. Gjestland discusses these factors of selection and adds to them the following observations on the Bruusgaard data: there is no information on treatment subsequent to 1910; information on many of the patients came from hospital records of admissions to the Municipal Hospital for a variety of diseases; information on some patients came from interviews rather than physical examinations; only a few had spinal fluid examinations; only 40 patients had been autopsied. Each of these factors adds to the highly selective nature of the Bruusgaard data. Despite their own warnings as to interpretations, authors of papers on the prognosis of untreated syphilis and authors of the leading textbooks of syphilology have presented these data as the most reliable material on the prognosis of untreated syphilis. Some authors have used these figures as a basis of comparison of the efficacy of treatment. Therefore, it is important that an effort be made to clarify the issue by a more complete study of the material.

The significance of the problem of untreated syphilis in current American practice is further emphasized by the fact that more than one-half of the persons (in the United States in the past decade) who acquire syphilis do not reach medical attention until after the early lesions have disappeared, some many years afterward, others not at all. American literature contains many statements lamenting this fact and pointing out that the golden opportunity for therapy in these

patients has been lost. It has been estimated by the U. S. Public Health Service that, as of Dec. 31, 1954, in the United States, there were approximately 2,000,000 persons whose blood, if tested, would be reactive for syphilis. Some of these have false positive tests but for those with untreated syphilis, some indication of their fate may come from this study. It is important, also, that although an estimated 86,800 United States civilians acquired syphilis in fiscal 1954, less than 10 per cent of these (7,688) were reported and treated for primary and secondary syphilis.[10] Every year more persons in the United States are diagnosed as having early latent syphilis than are diagnosed as having primary and secondary syphilis, and each year this ratio is increasing, meaning that relatively more each year remain untreated for primary and secondary syphilis. In 1954 the ratio of early latent (24,999 reported cases) to primary and secondary (7,688 reported cases) was approximately 3.5 to 1; in 1946 it was 1 to 1.

Another important fact in the significance of this problem is the evidence, both by clinical observation on man and laboratory experiments on animals, that syphilis in some way affects morbidity and mortality, aside from the late effects of the disease itself.[11] Thus, there appears to be considerably greater morbidity among untreated syphilitics and, in addition, life is shortened appreciably due to other conditions than manifestations of late syphilis.

Of prime importance in determining the potential contribution of this investigation was to examine the diagnostic criteria of those times and analyze the validity of the diagnoses made in Boeck's department. These diagnoses were based entirely on clinical examination and subsequent observation (because neither darkfield nor serologic tests for syphilis were employed in Oslo before 1910). A large sample of the hospital records have been examined carefully by the authors of this review (E.G.C. and N.D.) and in their opinions there is no doubt that a great majority of these patients had early syphilis. The potential margin of error of conventional clinical admission diagnoses was reduced significantly by observations on the daily course of the untreated disease over periods of months in all patients. These patients were hospitalized from their first tentative admission diagnosis until all signs and symptoms disappeared (an average of 3.6 months, Table II), many of them (42.6 per cent of males and 20.5 per cent of females) having primary and secondary syphilis on admission or developing secondaries after primary lesions had disappeared. One-half of the males and three-fourths of the females were observed with secondary syphilis only (see Fig. 1). Furthermore, Boeck was an expert of international reputation and his deputies were experienced dermatosyphilologists, all trained in the highly developed art of clinical description of the times. The necessity for accurate diagnosis was further increased by the requirements of a good teaching hospital.

Table II shows the length of stay of patients in the hospital, 39 of the patients remaining in the hospital for as long as 10 to 12 months. The mean stay in months for males was 2.7 and for females 3.9. Of interest is the considerably longer hospitalization of the females than of the males. Whether this means that the lesions of females persist longer than those of males or whether for the control of infectiousness, it seemed better to hospitalize the females longer,

cannot be determined, but it is possible that this is an early indication of the difference in the response of males and females to this infection. This lengthy hospitalization of both sexes illustrates the long duration of early syphilis lesions and emphasizes the potential dangers of untreated syphilis in a population.

TABLE II. STUDY GROUP—NUMBER OF MONTHS IN HOSPITAL AND MEAN HOSPITAL STAY ACCORDING TO SEX

MONTHS	MALE	FEMALE	TOTAL
3 and under	280	379	659
4 to 6	142	435	577
7 to 9	19	110	129
10 to 12	5	34	39
			1,404
Mean stay in months	2.7	3.9	3.6

Adapted from Gjestland, Chapter III.

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Fig. 1* shows the distribution of the patients in the study group† by stage of disease and sex. The diagnoses are those confirmed at discharge, after the patients had been under observation throughout the period of hospitalization. In only seven instances is the diagnosis limited to primary syphilis. Of these, three did not develop secondary syphilis while in the hospital and four were discharged against advice before their lesions were healed. The classification "primary *and* secondary syphilis" includes those who were admitted with primary lesions and developed secondary syphilis while in the hospital, together with those who were admitted with primary and secondary lesions. The largest group were those with secondary syphilis, having been admitted in this stage. The primary *and* secondary group comprised a higher percentage of males than females (42.6 versus 20.5), a proportion in accordance with the general experience of later diagnosis of early syphilis in females. The largest proportion of females was in the secondary syphilis group, the diagnosis having been made after the disappearance of primary syphilis, or in some instances without a history of primary syphilis at all. Approximately 5 per cent of the patients were admitted in clinical secondary relapse. This group represents patients previously observed elsewhere for secondary syphilis, with or without treatment, whose symptoms and signs had disappeared only to reappear with manifestations characteristic of secondary relapse.

The aims of Gjestland's study were stated as follows: "Based upon the concept of disease as a process, an attempt will be made to show the natural course of syphilis according to as many indices as the material will allow, and thereby contribute to a better understanding of the prognosis and perhaps establish a base line for the interpretation of the huge mass of information we

*Figs. 1-13 have been constructed by one of us (E. G. C.) from the detailed tabular material provided by Gjestland.

†See page 319 for description of study group.

already possess."[1] The immediate objectives for reaching these aims were formulated as follows: "1. To trace as many patients as possible to an 'end point,' defined as the last observation, living or dead; 2. To collect the maximum amount of clinical data (including data on treatment) on each patient from the date of his original discharge from Boeck's department all through the interim period and up to the 'end point'; 3. To determine the causes of death through a study of post-mortem examinations, hospitalizations, death certificates, etc., with the maximum amount of accuracy; 4. To examine at the Rikshospitalet as many living patients as possible and to employ as complete examinations for syphilis as circumstances will permit and to have examined elsewhere according to the same principles those patients who, for some reason or other, could not be brought to the Rikshospitalet."[1] The question asked from the beginning was: What is the final outcome in terms of late syphilis, duration of life, and cause of death in persons who are untreated for symptomatic early syphilis?

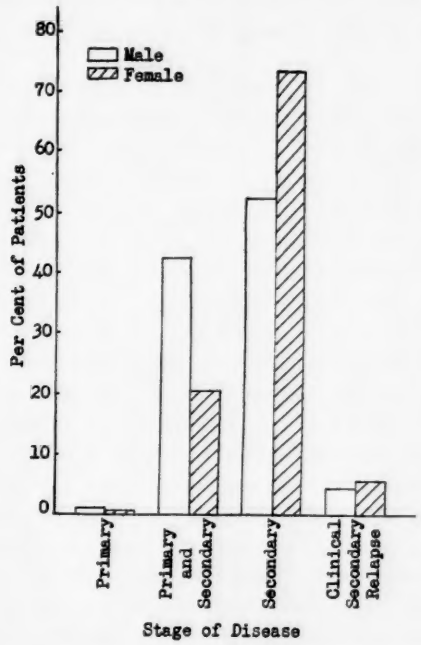

Fig. 1.—Distribution by stage and sex of the study group (1,404 Norwegian residents of Oslo). (See page 319 for description.)

II. APPRAISAL OF THE EXISTING INFORMATION BEARING ON THE SUBJECT

A critique of all of the pertinent literature obviously could not be made, because a subject so broad as the natural course of syphilis infection would require reference to practically the entire field of syphilology. Appraisals were limited to: (a) classification and critical evaluation of other investigations on the outcome of untreated syphilis, and (b) well-known authoritative reports dealing with the various aspects of syphilitic infection: secondary relapse, benign

late syphilis, cardiovascular syphilis, neurosyphilis, etc. Gjestland's evaluations of the literature on these specific aspects of syphilis infection in relation to his own data are among the worthwhile contributions of this investigation, particularly the presentation and evaluation of the essential items to consider when comparisons between studies are attempted. So frequently the results of one study are compared with the results of another, and because of similarities of numbers they are considered to support each other. This is often done without a consideration of the factors that go to make up the study material. Gjestland's monograph provides an excellent lesson in comparative analyses.

Most of the studies of untreated syphilis are based upon series of patients who are self-selected, either because of no knowledge of being infected or because of recalcitrance in following medical advice. Gjestland was able, from a search of the literature, to find only two groups who were denied treatment deliberately and these were left untreated for two totally different reasons: (a) the Boeck group, untreated because of a scientific conviction as to noneffectiveness of mercurial treatment, and (b) the "Alabama" group, left untreated for the purpose of comparing health and longevity of an untreated syphilitic population with an otherwise similar but nonsyphilitic population.[11-15]

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There are at least four methods or techniques by which information on the outcome of untreated syphilis has been acquired: (a) from anamnestic data, obtained from patients seen for the first time in latency or in the late symptomatic stages of the disease; (b) from autopsy studies, such as those of Rosahn[17,18]; (c) from prospective "no treatment" studies, such as the "Alabama" series (loc. cit.); (d) from specific groups of patients known to have been denied treatment in the past (e.g., Bruusgaard study of the Boeck patients).

"Each of these four techniques is fraught with sources of potential bias and these should be carefully considered in making statements about the prognosis of untreated syphilis. The shortcomings of the first technique, which, incidentally, is more frequently used than any of the others, are quite apparent. The patients are highly selected and the groups studied rarely include patients whose courses were so benign as to require no medical attention."[1] None of the anamnestic studies is critically appraised by Gjestland, but evaluations of the other three types are made in considerable detail. These details will not be presented in the present review, except to point out the similarity between the figures of Rosahn and those of Bruusgaard, despite the fact that the basic data are not comparable in any respect. Rosahn's patients were drawn from a hospital population of several types of patients, whereas the Bruusgaard group came from a hospitalized syphilitic population. Bruusgaard's included both the living and the dead, whereas Rosahn's comprised only those examined at autopsy. Only 8.5 per cent of the Bruusgaard group came to autopsy. The Bruusgaard material comprised 64 per cent females, whereas the Rosahn material was 35 per cent females. The findings were not expressed on a sex specific basis. The Bruusgaard material included several forms of late central nervous system syphilis and benign late syphilis, whereas the Rosahn material included neither benign late syphilis of the skin, mucous membranes, or bones, nor general paresis. The presentation of facts such as these, so critical for valid comparisons, illustrates another important contribution of the Gjestland monograph.

III. FORMULATION OF HYPOTHESES

Following an appraisal of the most pertinent literature, a careful study of the Boeck records, and a detailed and critical appraisal of Bruusgaard's results, the next step was to consider the specific questions for which the Boeck data might provide answers as follows: among patients untreated for secondary syphilis and with no, some, or unknown subsequent treatment: (1) What are the frequencies of secondary relapse, of benign late syphilis, of late symptomatic syphilis, of life long latency, and of spontaneous cure? (2) What are the effects on longevity, on causes of death, and on mortality over that of nonsyphilitics? (3) Does age at time of infection influence outcome? (4) Does sex influence outcome? (5) What are the effects on the outcome of pregnancy at varying intervals following infection? (6) Is morbidity from conditions other than syphilis greater than among nonsyphilitics?

"None of these questions have been omitted from consideration during the course of tracing and in the analysis of the data, but as the study progressed it became obvious that answers could not be provided for each and every one of them. The reasons for this lie in the material itself and in the extent to which complementary data could be obtained."[1]

On the basis of these questions and on the appraisal of pertinent literature, the study was designed to provide support or denial of the following hypotheses: (1) Syphilis, untreated in its primary and secondary stages, has a favorable outcome in a majority of instances. (2) Serious results are more frequent in males than in females. (3) Untreated syphilis prolongs the period of community danger of infection. (4) There is no way to predict the outcome in individual cases. (5) Syphilitics have a higher morbidity and mortality from other conditions than do nonsyphilitics.

It seemed reasonable at the outset that these five hypotheses were testable directly or indirectly with the Boeck patients, if a sufficient proportion could be traced and information secured on their clinical outcome. There was some doubt that sufficient information would be obtained to verify hypothesis number five; this proved to be partially true.

IV. TESTING OF HYPOTHESES

This step in the continuum of the epidemiologic method is the actual planning and execution of the design of the field investigation. It includes: the selection of the study group; the listing of possible sources of information; a plan for orderly tracing; a decision as to the method of collecting and recording data; a consideration of possible controls; and the actual collection and analysis of data.

Design of Investigation.—The study group finally decided upon comprised 1,404 individuals drawn from Boeck's original series of hospitalized patients. It may be recalled that the Bruusgaard study related to 473 persons of a total of 2,181 patients. On examination of the original records it was found that only 1,978 patients, rather than 2,181, were admitted between Jan. 1, 1891, and Dec. 31, 1910. This discrepancy is explained on the basis of duplicate entries and the possible inclusion of other stages and doubtful diagnosis in the registry

from which Bruusgaard's count was made. It is possible also that Bruusgaard's list included a few patients discharged during the year 1890. The 1,978 was reduced to 1,404 by the elimination of 574 Norwegian nonresidents of Oslo and non-Norwegians. It was believed that limiting the tracing to Norwegian residents of Oslo would not bias the over-all study and at the same time would simplify tracing and aid in the selection of controls. The decision to eliminate the 574 persons was made after a careful field study of a random 20 per cent sample of Boeck's original patients.

The remaining 1,404 Norwegian residents of Oslo came from the underprivileged section of society which at that time lived in the east zone of the city. Approximately 62 per cent were referred by the Bureau of Indigents, approximately a third by the Venereal Disease Division of the Oslo City Health Department, and a very small proportion came of their own accord to Boeck's clinic. A great majority (68 per cent) was admitted during the period 1891-1900. Only 10 per cent of the total group were admitted during the last five years of the period under study (1906-1910). The decreasing admissions to Boeck's clinic, year by year from 1891 to 1910, is parallel to the downward trend of actual notified cases in the city of Oslo, indicating that the smaller proportions admitted in the later years are the reflection of the declining syphilis problem, rather than a specific selection of the group coming to medical care.

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Fig. 2 illustrates the sex and age distribution of the study group. There were twice as many females as males, perhaps due to the relative numbers of male and female beds on the dermatology service. The ratio of males to females among notified cases in the city of Oslo was 2 to 1. The sex differences made it essential that all of the analyses throughout the entire study be made on a sex specific basis. Among both males and females the highest proportions were among the 15-24 age groups (46.7 per cent and 61.7 per cent, respectively) and the next highest among those 25-39 years of age (38.3 and 28.0 per cent). The mean age for the total group is 24.8 years with a mean of 25.6 and 24.3 years for males and females, respectively. The patients under the age of 15 acquired syphilis in the home, usually from another member of the family. They were often admitted to the hospital together with their mothers or fathers, or both, and occasionally together with one or more brothers or sisters. In many instances the whole family group suffered from secondary syphilis. The stage of disease by sex was shown in Fig. 1.

Careful examinations of the original records were made in order to determine the exact amount of treatment, that these patients received before, during, or *immediately** after discharge by Boeck. The vast majority of the patients (96.4 per cent) received no specific treatment whatever during the early stages of the disease and there are no appreciable differences between the sexes in this respect. The 3.6 per cent who received mercury in one form or another (inunctions, mercury pills, and mercury baths) received minimal amounts, only six men and nine women receiving more than 30 inunctions. Of the 50 patients who received mercury in one form or another, only three were treated by Boeck himself, the remainder having been treated before admission to Boeck's department, or immediately after discharge from it.

*Treatment received in later years is shown in Tables IV and V.

The complete plan of investigation cannot be given in detail here, but the thoroughness with which this plan was considered and undertaken and the method of search and identification is a model example of thoroughness. Two essential preliminary requirements for retrospective studies of this kind are the establishment of a "search order" and a system of identification of name and recorded data. A "search order" is a listing of possible sources of information in prearranged order which will assure a minimum of duplication of effort and, if followed routinely, will add a considerable degree of accuracy to the identifying process. Every name should be searched through the entire list even when it appears to have been located in the first source searched. Similarities of name and other identifying data make this necessary. Identity can be established objectively only by comparing a number of personal, geographic and clinical characteristics each time new information is found.

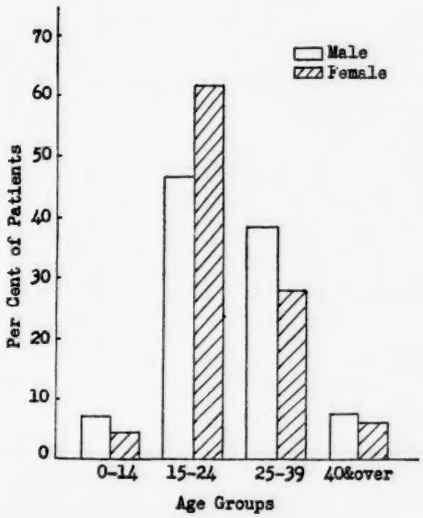

Fig. 2.—Distribution by age and sex of the study group (446 males and 958 females). Mean age: males, 25.6 years; females, 24.3 years.

Initial explorations were made on small samples of the total group in an attempt to discover the various sources where information might be obtained and the order in which the search should be made. Furthermore, a plan was devised whereby the identifying information found in one record could be checked objectively with that of another record by use of a special form and by following a fixed pattern. Every new record found in the tracing process presented problems of identity.

A list of the sources of identifying and clinical information, arranged in the order in which they were searched, is given here. This is the "Search Order" through which each name was taken. Only minor exceptions were made in this orderly and objective plan.

THE "SEARCH ORDER"

Chief Sources of Information and Order of Search *

1. Death registers.
2. The Department of Dermatology and Venereology of the Rikshospitalet.
3. The Oslo Bureau of Indigents.
4.† Bureaus of Indigents elsewhere.
5. The Central Bureau of Statistics' Marriage Registry for Oslo (women only).
6. The Oslo Population Register.
7. The Oslo City Health Department, Venereal Disease Division.
8. The Municipal Hospital at Oslo, Venereal Disease Division.
9.† Parish minister, sheriff, or local Population Register at patient's place of birth.
10.† Parish minister, sheriff, or local Population Register at patient's place of residence prior to his settling in the City of Oslo.
11.† Individual sources, especially relatives of the patient, but also many others not specified.
12. The Oslo City Health Department and the Central Bureau of Statistics (for transcription of death certificates).
13. Mental hospitals, psychiatric wards, neurological and other hospital wards (private practitioners as indicated).

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In addition to the small exploratory samples noted above, a 20 per cent representative sample of the 1,978 original patients, obtained by the use of random sampling numbers, was chosen and carefully investigated to test the record system and tracing procedures and to determine the practicality of studying the entire material. An analysis of this sample by Gjestland and a special committee‡ led to a decision to follow the entire study group along the same lines established through experience with the sample. The decision to include only those who were Norwegian residents of Oslo in 1890-1910 was supported by the evaluation of the sample.

It would have been interesting, and perhaps useful as well, to have traced as "controls" a similar group of nonsyphilitics and one of presumably adequately treated syphilitics. This was not done because an adequately treated group was not available and because it did not seem that the hypotheses being tested required such "control" groups. Considered as possible controls was a sample of contemporary nonsyphilitic, clinic or hospital patients, or a sample of contemporary admitting agency clientele. The decision against this was based upon the premise that only questions relating to cause and effect would absolutely require controls. Furthermore, there was the practical consideration of the availability of records and of time and resources to search them. The control which seemed most feasible under the circumstances was a comparison of the life experience of the untreated syphilitics with that of the local population from

*Adapted from Gjestland. Recheck sources omitted.

†These are supplemental sources.

‡The collected data on the sample was brought to this country by Danbolt and Gjestland in 1950 and reviewed by a committee composed of J. E. Moore, Niels Danbolt, Margaret Merrill (Associate Professor of Biostatistics, Johns Hopkins University), A. P. Iskrant (Chief Statistician, U. S. Public Health Service), Geraldine A. Gleeson (Statistician, U. S. Public Health Service), and E. Gurney Clark.

which they came. The study group was limited largely to patients residing in the eastern districts of the city of Oslo. There are official mortality records in Oslo by district so that it was possible to compare the mortality experience of untreated syphilitics with that of a population of the same socioeconomic status. For the details of the selection and study of the control group, reference must be made to the original monograph.

Collection of Data.—With a limited staff (Gjestland, a nurse-secretary, and a filing secretary), the tracing procedure began in 1949. From time to time the operation required and received the cooperation of various hospital staffs and many persons employed in the official record bureaus of the country. The magnitude of the job to be done did not detract from the attention to essential details. Every bit of information found on every patient was checked according to the identification plan, and all records (hospital and others) were recorded in toto in the master record folder. The record system, organized before the tracing began, comprised: (a) an index card file which served as a key to the other files and an index of the current status of tracing on each patient; (b) a master folder which contained the transcribed records from hospitals, admitting agencies, and physicians' offices; and (c) a summary record devised to permit analysis of the material as efficiently as possible in terms of the proposed questions and to give information on the natural course of syphilis infection.

At the close of the investigation in August, 1951, some usable information had been obtained on about 80 per cent of the study group of 1,404 persons. This corresponds very closely with the estimates of the 20 per cent sample and justified the use of the exploratory sample. In Table III and Fig. 3 are the results of the tracing efforts.

TABLE III. STUDY GROUP—TRACING STATUS, 1951, BY SEX "KNOWN," PARTIALLY "KNOWN," AND "UNKNOWN"*

TRACING STATUS	MALE		FEMALE		TOTAL	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
"KNOWN" LIVING	72	16.1	187	19.5	259	18.4
"KNOWN" DEAD	259	58.1	435	45.4	694	49.4
Subtotal	331	74.2	622	64.9	953	67.9
"PARTIALLY KNOWN"	43	9.6	151	15.8	194	13.8
Subtotal	374	83.9	773	80.7	1,147	81.7
"UNKNOWN"	72	16.1	185	19.3	257	18.3
TOTAL	446	100.0	958	100.0	1,404	100.0

From Gjestland, Chapter V.
*Defined in text.

The "known" group comprises those on whom a diagnosis could be established at a classifiable "end point." They were alive and examined during the investigation period; or, if dead, the time and status at death could be determined.

"Partially known" refers to those with one or more observations during the years following discharge from Boeck's department, but not to the same clear-cut "end points" of diagnosis as those of the "knowns." "Unknown" means no information following discharge from Boeck's department. For 83.9 per cent of the males and for 80.7 per cent of the females there was some significant information. Still alive in 1951 were 16.1 per cent of males and 19.5 of females. No follow-up information was available on 16.1 per cent and 19.3 per cent respectively. This is a high and probably unique degree of success in tracing a population group some 40 to 60 years after the original event. It is even more remarkable when one considers the mobility of the class of population from which these patients came, and the fact pointed out by Harrison[6] that during the period 1891-1920 there were 351,915 Norwegians (80 per cent of whom were in the ages 16-35) who migrated to the United States. The population of Norway in 1900 was 2,242,995.

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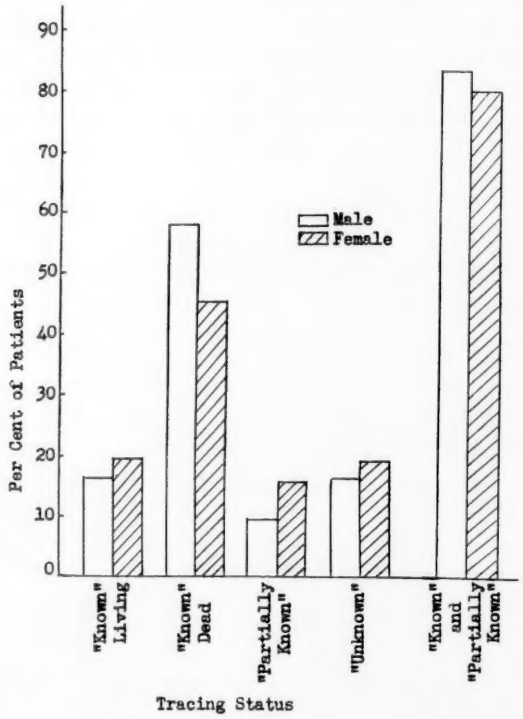

Fig. 3.—Tracing status in 1951 by sex.

The quantity and the quality of the information obtained on the "knowns" and "partially knowns" may be judged in part from the number of recorded observations and from an analysis of the sources of information at or just before death. On the 953 persons classed as "known" there were 3,584 recorded observations (an average of 3.8 per person), and on the 194 "partially known" 523

observations (2.7 per person), the over-all average being 3.6 observations. Of the "knowns" 259 were still alive (Table III) and of these 83.4 per cent were examined in Norway or elsewhere during or shortly prior to the period of investigation (1949-1951). For the remaining 16.4 per cent (43 persons) information was obtained directly or indirectly as to their health status. None were seriously ill, but complete examinations are not available. Information on the dead (694 persons) came from physical examinations immediately prior to death in approximately 29 per cent, from autopsy examinations in 30 per cent, from physical examinations a short time prior to death in 15 per cent, and from death certificates or other sources in 26 per cent.

A comparison of the 953 "known" and the 194 "partially known" with the total study group (1,404) according to original diagnosis, sex, and age groups and mean age revealed such similarity that it can be concluded that the "knowns" and "partially knowns" combined are definitely representative of the total as regards these variables.

An analysis of the amount, type, and time of treatment received by these patients during the 40 to 60 years since their discharge is important if valid information is to be forthcoming about the natural course of untreated syphilis. However, lack of complete information about treatment would not detract entirely from the practical value of this investigation. It is certain that no treatment was received for *early* syphilis by these patients, and what happens to such patients regardless of subsequent therapy is a subject of great interest. This is the situation which obtains for a large number of persons who annually pass untreated through early syphilis infection and who are candidates for discovery and varying amounts of treatment during the years that follow. An estimate of the possible outcomes in such persons with no or varying amounts of treatment is a major contribution of this study. This does not mean that the findings of the study have universal application to all similar situations, but no one will deny that the report provides useful information which does not exist elsewhere.

From the information available, Gjestland carefully analyzed the possible effect of treatment on the course of the disease in these patients. It was not possible to determine the exact treatment history for the majority, but it was possible to introduce a chain of circumstances which provide evidence that any treatment received was highly inadequate as judged by acceptable standards. "This evidence, both circumstantial and factual, is convincing and consists of two parts: (a) the historical development of *available* adequate treatment; and (b) the actual amount of treatment known to have been received by our patients."[1]

Two tables adapted from those of the monograph are presented here. Table IV shows the possibilities for specific treatment in Norway from 1891 to the present. These are the treatment schemes for "fresh" syphilis rather than for later stages. Before 1920, patients with latent or late syphilis were usually treated symptomatically and rarely, if ever, given as much treatment as is described in Table IV. Beginning about 1930, when Boeck's patients had had syphilis for 20 to 40 years, the practice in Norway (and elsewhere) changed and more extensive treatment was given at all stages of the disease.

TABLE IV. POSSIBILITIES FOR SPECIFIC TREATMENT IN NORWAY 1891 TO PRESENT

DATES	TYPE	COMMENT
1891–1910	Mercury alone	Rubs, pills, baths; amount based on clinical response
1911–1920	Arsenicals and mercury	Alone or combined, 3-6 injections, rarely more
1921–1930	Arsenic, mercury, bismuth	Combinations, courses 12-15 injections as plus 80-100 Hg. Bi infrequent
1931–1946	Arsenic, mercury, bismuth	Courses 16 As, 16 Bi, repeated 2 or more times, serologic control
1947–	Arsenic, bismuth, penicillin	Penicillin first in 1947, combined with As and Bi until 1950, then alone

Adapted from Gjestland, Chapter V.

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The amounts of treatment known to have been received are shown in Table V. In 83.4 per cent there was no treatment or no information as to treatment. Of those whose treatment histories were adequate, 15 patients (10 per cent of the treated, less than 1 per cent of the total) received 40 or more treatments; 86 (50 per cent of the treated, 6 per cent of the total) received less than 10 treatments (1 bismuth unit equals 6 mercury inunctions). In the majority of instances the treatment was received irregularly over periods of many years. "To what

TABLE V. INFORMATION ON ACTUAL TREATMENT RECEIVED FROM ONSET OF DISEASE TO "END POINT" BY SEX AND AMOUNT

STATUS	MALE		FEMALE		TOTAL	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
No information as to treatment, or no treatment	276	83.4	519	83.5	795	83.4
Patients found to have received treatment No. of As and/or Bi Units						
40 and over	4		11		15	
20–39	9		15		24	
10–19	14		19		33	
Subtotal	27	8.2	45	7.2	72	7.6
1– 9	28	8.4	58	9.3	86	9.0
TOTAL	331	100.0	622	100.0	953	100.0

From Gjestland, Chapter V.

extent the treatment given has affected the end results, however, is close to impossible to determine, but the problems will be dealt with in considerably more detail in the following sections on the various complications."[1]

V. CONCLUSIONS AND PRACTICAL APPLICATIONS

In conformity with the requirements of this final step, the collected and analyzed data are presented to show the extent to which the questions have been answered and the hypotheses verified for practical use. The results are given and discussed under the following chapter headings in the monograph: Clinical Secondary Relapse; "Benign" Tertiary Syphilis; Cardiovascular Syphilis; Neurosyphilis; Other Late Syphilis; Mortality; The Prognostic Significance of Clinical Secondary Relapse and "Benign" Tertiary Syphilis; and Spontaneous Cure. A consistent pattern is followed by the author in each chapter: excerpts and comments from the pertinent literature; the findings of the present study; and comparisons and discussions. In addition, there are ten annexes of tables, charts, analyses, discussions of a technical and explanatory nature, and exhibits. Only brief and incomplete presentations of these results can be made in this paper. For details reference must be made to the monograph itself or to the abbreviated version which will be available eventually.

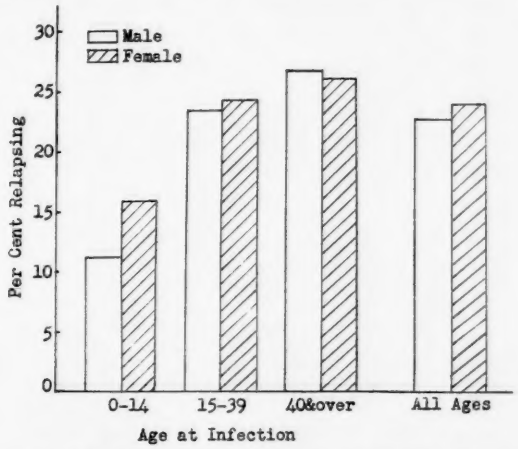

Fig. 4.—Clinical Secondary Relapse. Occurrence among 1,035 "knowns" and "partially knowns" by age at infection and sex.

Clinical Secondary Relapse.—This is one of the most significant of the analytical sections, contributing much to knowledge of the natural course of syphilis, so much, in fact, that the entire concept of relapse may be modified as a result of these findings. Although the opinion is not universal, much of the modern literature states that clinical secondary relapse is a phenomenon related only to inadequate treatment of early syphilis or must be regarded as progression. On the other hand, Meirowsky and Pinkus,[19] quoted by Gjestland, subscribe to Fournier's idea and emphasize the rhythmic course of syphilis infection unrelated to treatment. The Oslo study shows conclusively that clinical secondary relapse occurs in the absence of treatment. Approximately 25 per cent of these subjects experienced this phenomenon, and of these about one-fourth had multiple episodes. Figs. 4, 5, and 6 give data on the frequency and probability of secondary

relapse. Figs. 4 and 6 include the "known" and "partially known" of Table III (374 males and 773 females) from which have been removed those originally admitted *in* secondary relapse (Fig. 1) and those known to have received any kind of specific treatment before, during, or immediately after hospitalization by Boeck.

Fig. 4 shows the occurrence of *observed* clinical secondary relapse according to sex and age. None of these patients had received any treatment prior to the relapse. There are no differences between the sexes, and the lower proportion in the 0-14 age group is well within chance variation. Among the 244 patients (23.6 per cent of 1,035) who developed relapse, 46 (18.9 per cent) experienced two, 8 (3.3 per cent) three, and 1 (0.4 per cent) four, outbreaks; i.e., multiple outbreaks occurred in 22.5 per cent. Furthermore, both from the clinical and public health standpoint it is important to note that in 85 per cent of instances the relapsing lesions involved the mouth, throat, or anogenital regions.

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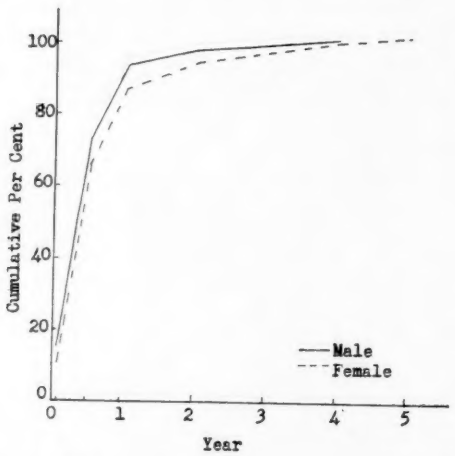

Fig. 5.—Clinical Secondary Relapse. Cumulative per cent by sex of those relapsing according to time interval between healing and observed relapse.

Fig. 5 shows graphs by sex of the cumulative percentages of those developing infectious relapse by time interval from healing of secondaries to first observed relapse. These results are similar to those presented by the Clinical Cooperative Group for inadequately treated patients. More than two-thirds of the relapsers had relapsed by the end of six months (males 72.3 per cent, females 65.1 per cent); by the end of a year, 92.3 per cent and 86.6 per cent; at two years, 96.9 per cent and 93.3 per cent; and by the end of five years, 100 per cent.

Fig. 6 shows the cumulative probability of developing the first outbreak of clinical secondary relapse among the Boeck patients. There is no appreciable difference between males and females, the probability being 22.5 per cent and 21.3 per cent by the end of the first year, and 24.3 and 24.8 per cent by the end of the fifth year.

The following quotation summarizes the author's conclusions: "It has been shown that symptoms and signs in untreated *secondary syphilis** disappear after a period of a few weeks to twelve months. This is then followed by a period of clinical latency, which in a minimum of 25 per cent of the cases is interrupted by new demonstrable lesions, or symptoms and signs of clinical secondary relapse. Of these patients again, a little more than one-fifth will experience from one to three additional outbreaks, likewise occurring after periods of clinical latency. *This development, therefore, must be considered as part of the natural course of the disease.** It has been held that the reaction of the skin and the mucosal membranes (and probably also of the eye, the bones, etc.) is dependent upon the multiplication of the spirochaetes at any given time, the rate of which is in turn determined by the status of the struggle between the immune forces of the body and the invading organisms. In our relapsers, the immune forces presumably have not been able to subdue the multiplication of the spirochaetes sufficiently to prevent a new crop of lesions from developing, the majority of which are infectious or potentially infectious. In other words, the theory held by so many

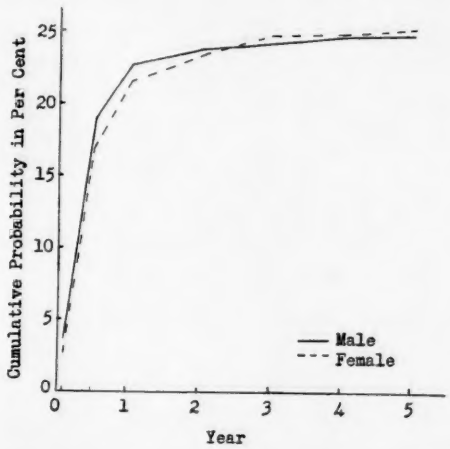

Fig. 6.—Clinical Secondary Relapse. Cumulative probability of developing in per cent, by sex, after healing.

modern syphilologists, that clinical secondary relapse is in itself mainly caused by inadequate or irregular treatment which interrupts the natural development of 'immunity,' has not been confirmed. If unsuccessful treatment of *secondary syphilis** results in the development of a certain percentage of relapses, it could better be put this way: The treatment has not been sufficiently adequate to prevent the natural course of the disease as expressed by the occurrence of clinical secondary relapse. Whether irregular or inadequate treatment during the secondary stage may result in a greater frequency of secondary relapse is a different matter, but so far there is no evidence pointing in this direction. On the contrary, it seems that under these circumstances even inadequate treatment is able to prevent secondary relapse to a certain extent."[1]

*Italics are Gjestland's.

Benign Tertiary Syphilis.—"The development of 'benign' tertiary lesions [benign late syphilis] is in general thought to be related to an upset in the parasite-host relationship resulting from reactivation of remaining treponemes in a sensitized host. That such a reaction in a sensitized host can result from treponemes introduced from sources outside the host is suggested by superinfection experiments in the laboratory and on man and by the observations of Grin[20] on endemic syphilis in Yugoslavia."[1] This statement introduces the section on benign late syphilis, defined as tertiary manifestations of the skin, mucous membranes, bones, and joints (exclusive of Charcot's joints). Gumma of the brain is classified under neurosyphilis and gumma of the liver under visceral syphilis.

Fig. 7.—Benign Late Syphilis. Per cent occurrence according to age at infection and sex

Figs. 7 and 8 and Table VI show the frequency and probability of "benign" tertiary syphilis. Fig. 7 gives the proportions developing this manifestation according to sex and age at time of infection. No statistically significant differences between the two sexes can be demonstrated, the males being higher in the 0-14 and the 40 and over age bands and the females higher in the 15-39 and in all ages (males 14.4 per cent and females 16.7 per cent). There is a tendency toward increasing proportions with age, but the differences are well within chance variation. Of those observed with benign late syphilis, 25 per cent of the males and 34.7 per cent of the females had from two to seven episodes of this manifestation, showing again a rhythmic feature of this disease. Solitary (single structure) lesions were more common (90 per cent) than multiple structure involvement; 70 per cent were skin, 9.6 per cent skeletal, and 10.3 per cent mucous membrane lesions. In the remaining 10 per cent which were multiple structure lesions, the skin was one of the structures involved in more than half of the instances.

Fig. 8 shows for 42 males and 115 females the cumulative percentages according to time interval since the healing of secondaries and the discovery of

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benign late lesions. Lesions developed from the first to the forty-sixth year, the majority developing by the end of the fifteenth year, and the mean duration of infection was 12.8 years in males and 11.2 years in females.

When the probabilities were calculated (Table VI), males and females showed significant differences at 15, 30, and 35 years, females being higher in each instance. This may indicate that the female agent-host equilibrium is disturbed earlier than that of males, and furthermore, may indicate actually a greater frequency of benign late syphilis in females, a finding not in keeping with what appears to be the case with later manifestations of this disease.

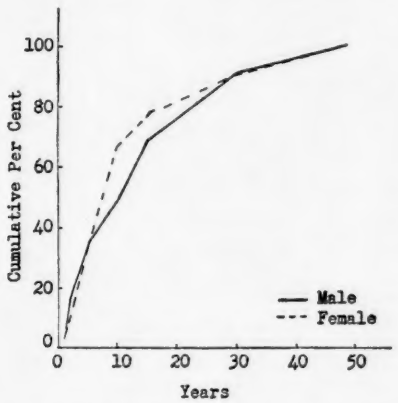

Fig. 8.—Benign Late Syphilis. Cumulative per cent by sex of those developing Benign Late Syphilis according to time interval from healing to observed lesions. Mean duration of infection, males 12.8; females 11.2 years.

TABLE VI. OUTCOME—BENIGN LATE SYPHILIS. PROBABILITY OF DEVELOPING B.L.S. CUMULATIVE, PER CENT, BY SEX

BY END OF	MALE	FEMALE
15 years	10.9	15.9
30 years	15.7	19.8
35 years	16.4	21.4

Adapted from Gjestland, Chapter VII.

Cardiovascular Syphilis.—It is not possible to present all of the details of this elaborate chapter of the monograph. Gjestland discusses many of the controversial and accepted features of this manifestation of syphilis, relating them to the data derived from his study. Of particular interest are those features having to do with diagnosis, duration of infection at time of diagnosis, sex differences, prognosis, and the relationship to occupation.

Only two tables (Tables VII and VIII) and two figures (Figs. 9 and 10) are presented here to illustrate some of the important features of this section. Fig. 9 gives the per cent of each age group and of all ages of the "known" 953 who were discovered to have developed some type of cardiovascular involve-

ment. Of particular interest is the fact that *none* of those infected before the age of 15 was found to have this type of late syphilis and, as expected in each age group, the proportions of males were significantly higher than those of females, the total rates for males being almost twice that for females, 13.6 per cent and 7.6 per cent, respectively. There was autopsy verification in 60 per cent, uncomplicated aortitis being discovered at autopsy in 22 of the 25 instances.

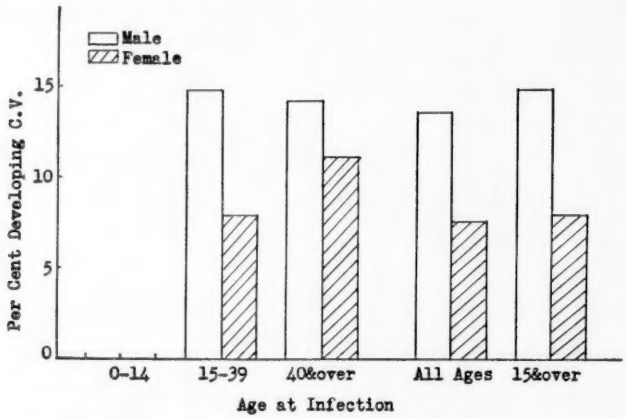

Fig. 9.—Cardiovascular Syphilis. Occurrence among 953 "knowns" by age at infection and sex.

Table VII gives the proportion of "knows" by sex and type (under age 15 excluded), who were observed to have developed cardiovascular syphilis, and the ratio of males to females for each type. Except for uncomplicated aortitis, where the ratio was 1 to 1, the ratio of males to females was 2 to 1 or greater.

TABLE VII. OUTCOME—CARDIOVASCULAR SYPHILIS. PROPORTION OF "KNOWNS" OBSERVED TO HAVE DEVELOPED CARDIOVASCULAR SYPHILIS BY FORM AND BY SEX (UNDER 15 REMOVED)

	303 MALES	584 FEMALES	887 TOTAL	RATIO M/F
Uncomplicated aortitis	2.6	2.9	2.8	1/1
Aortic insufficiency	7.3	3.3	4.6	2.2/1
Saccular aneurysm	3.6	1.5	2.3	2.4/1
Ostial stenosis	0.7	0.3	0.5	2.3/1
Aortitis—found at death	0.7	0.0	0.2	
Total complicated	12.3	5.1	7.6	2.4/1
TOTAL	14.9	8.0	10.4	1.9/1

Adapted from Gjestland, Chapter IX.

In Table VIII an attempt is made to give some suggestion as to possible minimum and maximum frequencies of cardiovascular syphilis by comparing the total "known" group with the autopsied population. Thus, it was suggested by Gjestland that the actual occurrence of uncomplicated aortitis among

TABLE VIII. OUTCOME—CARDIOVASCULAR SYPHILIS. COMPARISON OF "KNOWN" STUDY GROUP WITH AUTOPSIED PATIENTS

FORM OF CARDIOVASCULAR SYPHILIS	PER CENT IN STUDY GROUP	PER CENT IN AUTOPSIED GROUP
Uncomplicated Aortitis		
Males	2.6	9.3
Females	2.9	11.2
Complicated Forms		
Males	12.2	25.3
Females	5.1	10.4

Adapted from Gjestland, Chapter IX.

males may lie between 2.6 per cent and 9.3 per cent, and among females between 2.9 per cent and 11.2 per cent. The actual occurrence of the complicated forms may lie between 12.2 per cent and 25.3 per cent among males and between 5.1 per cent and 10.4 per cent among females. It was suggested further that the higher figure is the more likely one for the occurrence of uncomplicated aortitis, but that this is probably not the case in the complicated forms. These points can be clarified somewhat by a quotation as follows:

"It is obvious, for instance, that figures arrived at through the study of autopsy populations are not comparable with those found in ordinary follow-up studies. Any atuopsy population will necessarily be more or less heavily weighted with serious cases as compared with the hospital population from which it is drawn, and even more so as compared with the original 'syphilis universe.' This phenomenon was clearly demonstrated in our series, where the autopsied patients showed a considerably higher frequency of cardiovascular lesions than the study group as a whole. Moreover, if we consider the dead, the fact that about 66 per cent of those with cardiovascular involvement were found to have been autopsied, as compared with about 30 per cent of the total, shows that persons who had developed such complications ended up in hospitals *and** were submitted to autopsies to a far greater extent than were the others. When it comes to hospital populations, including a varying number of dead and living patients, materials selected from such groups also tend to become biased in the direction of more serious cases, because diseases brought the patient to the hospital, and thus figures arrived at in studies of this nature cannot be directly compared with those arrived at in follow-up studies. Finally, this is probably true as well of figures found in the studies of patients picked from hospitals *and** clinics (or outpatient departments), although not quite to the same degree as in the first two instances mentioned.

"Since the present investigation has all the characteristics of a follow-up study, it is hardly advisable to compare our quantitative data in respect to cardiovascular syphilis with those arrived at through the various other methods of approach just mentioned. As a matter of principle, therefore, we are in-

*Italics by Gjestland.

clined to consider it a prerequisite for such comparisons that the figures in question stem from a similar type of study. But this in itself is not a sufficient guarantee for comparability since methods of tracing, identification, and collection of clinical data may vary from one follow-up study to another according to geographical area, population groups involved, the investigator's attitude toward the problems, and other factors, all of which may have a considerable bearing on the end results. A critical evaluation of these factors and how they may have influenced the findings undoubtedly forms another requirement for eventual comparisons. The point is exemplified in our discussion of Aggerbeck's (1949) and Nielsen's (1950) Danish studies as well as in the analysis of our own data. Thus, only after having evaluated the basic epidemiologic methods employed in establishing the materials in question is it, in our opinion, worthwhile to proceed to a discussion of the many other factors involved, the most important of which are going to be considered in the following."[1]

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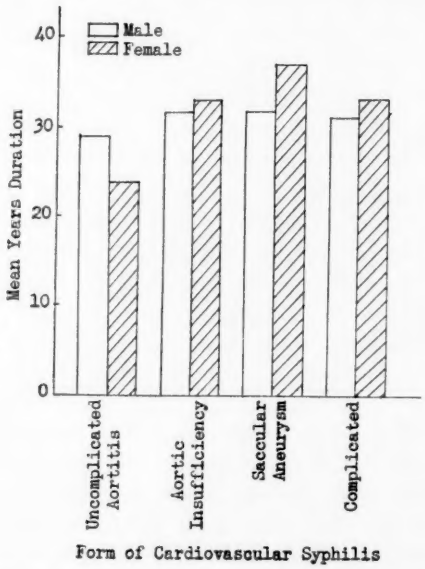

Fig. 10.—Cardiovascular Syphilis. Duration of infection at discovery, in mean years, by form and by sex.

Fig. 10 is constructed to show the duration of infection at the time of diagnosis of cardiovascular syphilis (not the onset of symptoms). In all forms except uncomplicated aortitis the diagnoses were made on the average in the fourth decade of infection. The numbers are small and the differences slight.

Neurosyphilis.—In this section of the monograph the data are presented as before with a consideration of the pertinent literature, the presentation of the data of this investigation, and a discussion of his own data as they relate to other information in the medical literature. The precautions to be observed in making comparisons of one set of figures with another is repeatedly emphasized. Figs. 11 and 12 and Table IX briefly review some of the information in this section.

Fig. 11 gives the proportion of each age and sex group and of all ages observed to have developed neurosyphilis by age at time of infection. Of the 62 persons who developed neurosyphilis, 31 were males and 31 females, whereas of the total "known" group the population of females was twice that of males. Neurosyphilis was observed in 9.4 per cent of the males and 5.0 per cent of the females. It is of interest here to note that neurosyphilis *did* develop among those infected under the age of 15. Of this age group 6.1 per cent developed neurosyphilis, with a male to female ratio of approximately 4 to 1. None of the 28 males over 40 at infection developed neurosyphilis, whereas 2 of 45 females did. It is to be noted also that this analysis includes only symptomatic forms; no asymptomatic neurosyphilis is included.

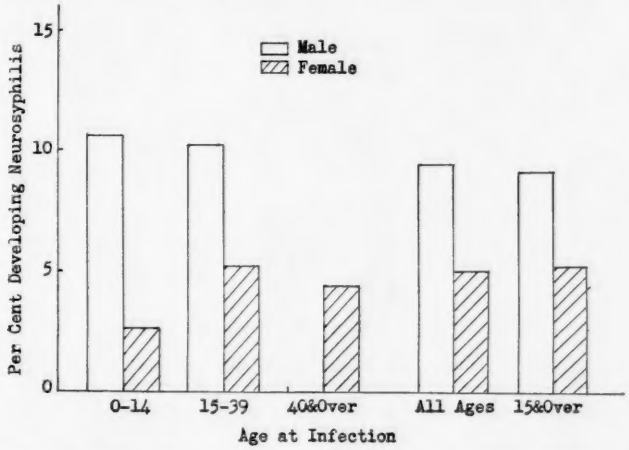

Fig. 11.—Neurosyphilis. Occurrence among 953 "knowns" by age at infection and sex.

Table IX shows the forms of neurosyphilis and the proportions of the "knowns" (of all ages) who developed each form. Also given is the ratio of males to females, and it can be seen that in each category the ratio is about the same, approximately 2 to 1. Of the 62 persons with neurosyphilis, 18 were alive and examined during the period of the investigation, these being equally divided among males and females. Of the dead, neurosyphilis was recorded as the primary cause of death in two-thirds of the instances. In the other third, neurosyphilis was present but unrelated to the causes of death.

TABLE IX. OUTCOME—NEUROSYPHILIS. PROPORTIONS OF "KNOWNS" OBSERVED TO HAVE DEVELOPED NEUROSYPHILIS BY FORM AND BY SEX—ALL AGES

	331 MALES	622 FEMALES	953 TOTAL	RATIO M/F
Diffuse meningovascular	3.6	1.7	2.3	1.9/1
General paresis	3.0	1.7	2.1	1.8/1
Tabes dorsalis	2.5	1.4	1.9	1.7/1
Gumma of brain	0.3	0.2	0.2	1.5/1
TOTAL	9.4	5.0	6.5	1.8/1

Adapted from Gjestland, Chapter VIII.

The duration of infection at the time of diagnosis is shown in Fig. 12, according to form and by sex. There is little difference between the sexes, except in general paresis where, on the average, the duration of the infection was less in females. The duration is shorter than that of cardiovascular syphilis and is in keeping with what is known about the natural course of this disease.

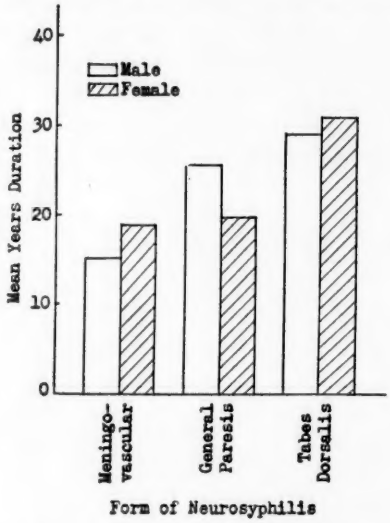

Fig. 12.—Neurosyphilis. Duration of infection at discovery, in mean years, by form and by sex.

Other Late Syphilis.—Out of 953 patients classified as "known," only two were found to have other types of late syphilis. Two females had gummas of the liver, one found at autopsy and one diagnosed clinically. In each instance the manifestation was considered to be the primary cause of death.

Mortality.—Two theories have been advanced to explain the excess mortality among syphilitics above that expected as a result of the late effects of the disease itself: (a) Syphilitics by and large come from a segment of the population characterized by high mortality rates from many causes as a result of low socioeconomic status; (b) syphilis as a generalized systemic disease exerts an adverse and nonspecific effect on most of the organ systems of the body.[11,13,14,21] The mortality of this series of patients was studied by Gjestland from three viewpoints: (a) the actual causes of death; (b) the probabilities of dying primarily as a result of syphilis infection; and (c) the excess mortality of syphilitics as compared with a control series.

Table X shows the primary causes of death among the 694 known dead. Syphilis was the primary cause of death in 15.1 per cent of the males and 8.3 per cent of the females, a ratio of 1.8 to 1. Among males, syphilis ranked second, and among females, fifth, as a cause of death. In each group tuberculosis led the causes of death, and in females more died of cancer and diseases of the circulatory and respiratory systems than of syphilis. Thus, among a 100 per cent syphilitic population 84.9 per cent of males and 91.7 per cent of females died of other causes.

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TABLE X. PRIMARY CAUSES OF DEATH BY SEX AMONG 694 KNOWN DEAD

PRIMARY CAUSES OF DEATH	MALES			FEMALES		
	NO.	PER CENT	RANK	NO.	PER CENT	RANK
Tuberculosis	45	17.4	1st	74	17.0	1st
Syphilis	39	15.1	2nd	36	8.3	5th
Cancer and other tumors	32	12.4	3rd	71	16.3	3rd
Diseases of circulatory system*	28	10.8	4th	72	16.6	2nd
Diseases of respiratory system*	25	9.7	5th	42	9.7	4th
Sudden—Unknown, Unspecified	20	7.7	6th	18	4.1	8th
Diseases of urinary and genital tract	16	6.2	7th	16	3.7	9th
Diseases of nervous system and sense organs*	14	5.4	8th	34	7.8	6th
Accidental deaths	11	4.2	9th	9	2.1	12th
Diseases of digestive system	7	2.7	10th	24	5.5	7th
ALL OTHERS	22	8.7		39	8.9	

Adapted from Gjestland, Chapter XII.
*Syphilis excluded.

The cumulative probability of dying directly as a result of syphilis was 17.1 per hundred in males and 8 per hundred in females by the end of 40 years of infection among this group of patients.

In order to study possible cause and effect relationships for the excess mortality of syphilitics over nonsyphilitics, a control group was chosen from the population of the city of Oslo for comparison with the mortality experience of Boeck's patients. It was found that most of his patients came from the eastern parishes of the city and their mortality experience could be compared by age, sex, and cause, and by decade with the population from which they came. This was studied in considerable detail and will be reported in a separate publication.[22] The findings reported in the monograph are shown in Table XI.

TABLE XI. MORTALITY. EXCESS IN SYPHILITICS AS COMPARED TO THAT EXPECTED ON BASIS OF EXPERIENCE OF RESIDENTS OF EASTERN PARISHES OF OSLO BY AGE AND SEX FROM 1890-1940*

AGE	MALES			FEMALES		
	EXPECTED DEATHS	OBSERVED DEATHS	EXCESS PER CENT	EXPECTED DEATHS	OBSERVED DEATHS	EXCESS PER CENT
10–19	2.3	1	0	4.4	5	14
20–29	13.7	15	9	29.4	42	43
30–39	21.5	33	53	43.1	84	95
40–49	24.8	55	122	36.8	69	88
50–59	30.5	48	57	38.3	60	57
60–69	28.4	41	44	26.6	41	54
70 and over	18.9	21	11	25.3	31	23
ALL AGES	140.1	214*	53	203.9	332*	63

Adapted from Gjestland, Chapter XII.
*Deaths after 1940 excluded. Decade included German occupation of Norway which influenced Norwegian population and mortality statistics.

This table shows that these untreated syphilitics had an excess in mortality over that expected of 53 per cent in males and 63 per cent in females (all ages), and there was some degree of excess in every age group except males 10-19. The excess was most pronounced in males 40-49 and in females 30-39. A similar picture of excess mortality was found when the mortality experiences of the eastern and western parishes were compared according to age, sex, and decade; the eastern group with lower economic status showed excess mortality over that of the west in practically every category of comparison. The average excess mortality of the east over the west (all ages) was 16 to 27 per cent among males and 25 to 38 per cent among females.

Gjestland concludes this section by expressing an opinion that although these results appear to lend confirmatory evidence to the nonspecific unidentified effect of syphilis infection on mortality, he does not believe that this is true. Additional quantitative support will doubtless be offered in the detailed study of mortality to be published later.[22] In the monograph he states that if these results are to be explained on the basis of this unknown factor, it must be assumed that it exerts its influence at all ages and at all durations, that its influence varies in different age groups, and that it exerts its effects through a number of other diseases in various organ systems. He cannot conceive of a mechanism that could work in this manner. He explains the excess mortality purely on a basis of lower socioeconomic status; and this seems reasonable in view of the similarity in the pattern of excess mortality when west is compared with east and the eastern population is compared with the Boeck patients. With decreasing socioeconomic status there are increasing risks of mortality from many diseases, and even within the lower strata there are perhaps some groups at greater risks than others.

Summary of Data on Outcome.—Fig. 13 gives a summary of the outcomes among the living and dead according to sex and shows that in this series of patients, as in many other series that have been reported, serious outcomes are more frequent among males than among females. The proportion of infectious relapses are about the same. A higher proportion of females than males developed benign late syphilis, but for cardiovascular and neurosyphilis the ratio of males to females is approximately 2 to 1. Similarly, syphilis as a primary cause of death gives a male:female ratio of 2 to 1. The varying numbers of patients upon which these proportions are based can be better understood by reference to Table III. Infectious relapse is based upon both the "known" and "partially known" group, less those treated and those seen originally in infectious relapse. Benign late includes the entire "known" and "partially known" groups. Cardiovascular and neurosyphilis are based upon the "knowns" only and the cause of death based on those in Table III known to be dead.

The Prognostic Significance of Clinical Secondary Relpase and "Benign" Tertiary Syphilis.—The prognostic significance of clinical secondary relapse was examined by dividing the patients by sex into two groups, those who were observed to have clinical secondary relapse and those who were not observed to have clinical secondary relapse. The occurrence of benign late syphilis,

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cardiovascular, and neurosyphilis was calculated for each of these two groups (table not shown here). There was considerable variation in both directions and in females there seemed to be a slight tendency toward more benign late syphilis and more neurosyphilis in the relapsers as compared with the nonrelapsers. This was not marked in males nor in the group as a whole (of relapsers 43 per cent had late syphilis, of nonrelapsers 39 per cent), and none of the differences were found to be statistically significant. Thus, from these data, there is no indication that the occurrence of clinical secondary relapse per se influenced the ultimate outcome of the disease among these patients untreated during primary and secondary syphilis.

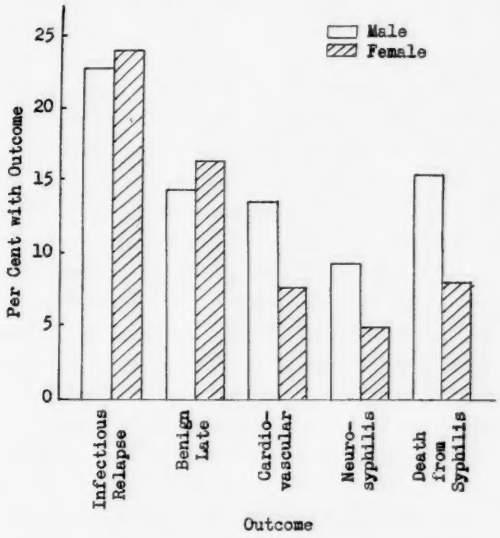

Fig. 13.—Summary of outcomes by sex.

Because of numerous references in the literature to the protective influence of benign late syphilis, Gjestland examined the prognostic significance of benign late syphilis from three standpoints: (a) concomitant benign late and other late syphilis; (b) the extent to which benign late preceded other late syphilis; and (c) the final outcome among those observed to develop benign late and those who did not.

Among his patients, concomitant or simultaneous benign late syphilis and cardiovascular syphilis occurred in 2 of 92 instances; benign late and neurosyphilis in 5 of 62 instances. This is what one would expect in view of the fact that the mean ages of development of these complications are so different. The extent to which cardiovascular and neurosyphilis were preceded by benign late syphilis was found to be no greater than the proportion of benign late syphilis in the study group as a whole (17 per cent of late syphilis had benign late, 16 per cent of the study group). The final outcome among those who had previously developed benign late syphilis and those who had not did not differ significantly in this series of patients (late syphilis was observed in approximately 21 per cent of those who had had benign late and in 16 per cent of those who

did not). "As the figures stand, therefore, and with the reservations made necessary by the small numbers involved, it is probably safe to state that the findings in the present series do not provide evidence for the concept that lesions of the skin, mucous membrane, and the bones in themselves exert a protective influence against serious late manifestations."[1]

Spontaneous Cure.—There are many statements in the literature about the frequency of spontaneous cure, but very little evidence is available to support the estimates. One of the barriers to an understanding of this problem is the strictness of definitions of spontaneous cure made by various authors. For the purposes of examining this problem in the Oslo material, a definition of spontaneous cure suggested by Moore in a personal communication to Gjestland and slightly modified by him was used. By this definition a diagnosis of spontaneous cure would have to be limited to those in a group of originally untreated syphilitics who (a) had shown no symptoms of syphilis after the early outbreak; (b) had received no specific treatment for latent syphilis during the interim period; (c) had been examined before death, with normal physical findings as far as syphilis was concerned and who then had a negative serologic test and normal spinal fluid; (d) had at autopsy shown no evidence of syphilis. It is safe to say that no representative group of patients satisfies these rigid criteria. The present study is no exception. The shortcomings in this respect of the Bruusgaard series and that of Rosahn are discussed thoroughly by Gjestland and, furthermore, details are given to show that the present data do not lend themselves to an analysis of this kind. It is doubtful that any material will ever become available which will satisfy these criteria. From a practical standpoint, however, in so far as individual patients are concerned, the important question is: To what extent does a group of untreated or highly inadequately treated syphilitics pass through life with little or no inconvenience as a result of the disease? The following quotation indicates an answer derived from the study of this material. "Out of every 100 patients 13 were found to have developed 'benign' tertiary alone, 15 were found to have developed cardiovascular and/or neurosyphilis, either alone or in various combinations; that is, a total of 28 were found to have developed some type of late manifestations. In other words, some 72 patients out of every 100 were found *not* to have developed any late lesions. In this connection it must be emphasized that our figures on the various complications to a certain extent were considered to be minimum. Therefore, the above figure of 72 out of every 100 patients is probably not representative. As mentioned previously, it is connected with considerable difficulties (sic) to estimate to what extent our figures for the various complications were minimum, but if we assume that somewhere between 60 and 70 (probably closer to 60 than to 70) out of every 100 untreated syphilitics in the present series went through life with little or no inconvenience as a result of the disease we are probably not too far from the truth."[1] It should be noted that 30 out of every 100 males were found to have developed some type of late lesions (including benign late syphilis) and 26 out of every 100 females developed such lesions.

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These figures (60 to 70 per cent not inconvenienced by untreated syphilitic infection) appear to confirm the estimates based upon Bruusgaard's material (Table I). From an epidemiologic point of view, however, the similarity of the figures is fortuitous since Bruusgaard's are based on an inadequate sample (about 20 per cent of the total) followed for relatively brief periods of time (many for less than 10 years and some of these unexamined) and not sex specific. The present study, on the other hand, involves an 80 per cent sample and a follow-up period of 40 to 60 years and analyzed on a sex-specific basis. While Bruusgaard limited himself to the presentation of his basic facts and drew no inferences therefrom, many subsequent workers did draw such inferences as to the prognosis of untreated syphilis based on their own and Bruusgaard's work. In spite of the fact that, as Harrison,[6-8] Sowder,[9] and now Gjestland[1] have shown, such inferences were unjustified, those who drew them are perhaps lucky to have so little to retract, since Gjestland's data thoroughly justify the prognostic estimates based upon the Bruusgaard material, despite the selected nature of his sample.

SUMMARY

Nowhere in the world is there a more unique opportunity to learn what happens when early syphilis goes untreated than from the files of Boeck of Oslo, Norway. His scientific conviction as to the inadequacies of the specific treatment of the day led him to withhold treatment from approximately 2,000 patients with primary and secondary syphilis during the twenty-year period, 1891-1910. Community protection from infection was aided by the hospitalization of these patients until all traces of the disease had disappeared (from 1 to 12 months, average 3.6 months). In 1929, his successor, E. Bruusgaard, reported on a follow-up study of 473 of these patients and provided information on the outcome of untreated syphilis, which has formed the basis for prognostic statements on syphilis for more than twenty-five years. Now, in the department of Bruusgaard's successor, Danbolt, the entire material has been restudied successfully by Gjestland.

This restudy represents a striking example of the application of the modern epidemiologic approach. In addition to the scientific contribution of this investigation, an outstanding illustration of international scientific cooperation has been demonstrated.

The remarkable degree of success in obtaining significant information on approximately 80 per cent of the study group, 1,404 Norwegian residents of Oslo of 1891-1910, was undoubtedly due to the careful planning which preceded the tracing efforts. This planning included: (a) a consideration of the nature, extent, and significance of the problem of untreated syphilis; (b) an appraisal of existing information on the subject; (c) the setting up of hypotheses to be tested and questions to be answered; and (d) a detailed outline for a practical experiment design. The pretracing experiment design comprised: the selection of the study group; the listing of possible sources of information; a plan for orderly tracing; a provision for the collection and recording of information; plans for "controls"; and an outline for the analysis of data. Of particular

importance is that these features of detailed planning preceded actual data collection. This characteristic of the epidemiologic method is well illustrated by this study.

The study was undertaken with the ultimate objective of providing information on the ". . . natural course of syphilis according to as many indices as the material will allow. . . ."[1] The questions originally asked of the material were: Among patients untreated for secondary syphilis and with no, some, or unknown subsequent treatment: 1. What are the frequencies of secondary relapse, of benign late syphilis, of late symptomatic syphilis, of lifelong latency, and of spontaneous cure? 2. What are the effects on longevity, on causes of death and on mortality over that of nonsyphilitics? 3. Does age at time of infection influence outcome? 4. Does sex influence outcome? 5. What are the effects on the outcome of pregnancy at varying intervals following infection? 6. Is morbidity from conditions other than syphilis greater than among nonsyphilitics?

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Analysis of this material provides useful information in reference to questions 1 to 4. Unfortunately, it was impossible to collect significant data for question 5 and the matter of congenital syphilis was postponed for future investigation on a more limited scale. Data relating to question 6 will be introduced in a subsequent publication[22] if satisfactory inferences can be drawn about morbidity from an extensive mortality study. The data relating to the remaining four questions are summarized in the following paragraphs.

One of the significant contributions of this investigation is the information obtained on clinical secondary relapse: 23.6 per cent of these patients experienced this manifestation within five years of discharge from the hospital (males 22.7 per cent, females 24.0 per cent) and of these approximately one-fourth had multiple episodes.

Benign late syphilis occurred in 14.4 per cent of males and 16.7 per cent of females. It was observed as early as the first year after discharge and as late as the forty-sixth year, the majority developing by the fifteenth year. There was some evidence of earlier appearance in females than in males and some suggestion that the probability of development is greater among females.

Cardiovascular syphilis was observed to have developed in 13.6 per cent of males and 7.6 per cent of females, no cases occurring in those infected before the age of 15.

Neurosyphilis did develop in patients who were infected before the age of 15 but not in males infected after the age of 40. In neurosyphilis there was a 2 to 1 ratio of males to females (males 9.4 per cent and females 5.0 per cent).

The mortality from syphilis among males was twice that of females, but in neither sex was it an important cause of death. It was second as a cause of death in males and fifth in females, but approximately 90 per cent of deaths were from other causes. There was a definite excess mortality among these syphilitics as compared to the population group from which they came.

No evidence was found to support the idea of the prognostic importance of either clinical secondary relapse or benign late syphilis.

The best definition of spontaneous cure is too rigid to permit quantitative evaluation. More practical is a consideration of the extent of disability during the lifetime of the persons involved. It was estimated that between 60 and 70 out of every 100 of these patients went through life with a minimum of inconvenience despite no treatment for early syphilis. This gives no encouragement to withhold treatment because the final outcome in any individual cannot be predicted, and, too, syphilis is still a transmissible disease when untreated and can cause serious difficulties among 30 to 40 out of each 100 who remain untreated.

This is probably the most comprehensive study of untreated syphilis that has yet been made, and the great mass of data that has been collected will provide the basis for additional contributions to our knowledge of syphilis infection. This brief review cannot do justice to this monumental piece of work comprising a monograph of some 500 pages, with 83 tables and 12 figures, and an annex of 70 pages with 30 tables and 2 figures. Gjestland's contribution will stand as a model of carefully planned and successfully executed field research and will provide the medical literature with the long awaited restudy of the Boeck-Bruusgaard material.

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Editorials

THE IMPORTANCE OF THE GENERAL PRACTITIONER IN CANCER DETECTION

CANCER unquestionably ranks as one of the major medical problems of our time. According to two current estimates, between one-fourth and one-third of the population will develop some form of cancer during their remaining lifetime.[1,2] The estimated cancer figures for 1955 are: new cases, 550,000; cases under treatment, 740,000; deaths, 235,000. These numbers may increase in future years as mortality from other diseases declines and the proportion of people in the older age groups becomes greater. A threefold approach to cancer control is called for: (1) prevention by identification of carcinogenic agents through field and laboratory studies and their effective removal from the environment; (2) development of new principles and techniques for cancer diagnosis and therapy; and (3) the more effective use of diagnostic and therapeutic measures now at hand.

The general practitioner plays the strategic role in present cancer detection efforts, since as a group, he comprises half of the medical fraternity. Moreover, he is usually the first physician to be visited by the average person seeking medical care. Control of this disease, taking into account the biologic variation in tumor growth, depends principally on early diagnosis and prompt, adequate treatment. It is therefore significant that half of all cancers are in sites accessible to direct examination by techniques and instruments already in the hands of physicians.[2]

In Connecticut, where a state-wide cancer register has been maintained for twenty years, an upward trend in five-year survival rates for all sites combined (from 22 per cent as of 1939, to 28 per cent as of 1948) has been noted.[3] Despite this encouraging trend, current improvement in survival prospects has not approached the goal of better than 50 per cent five-year survivals or cures thought attainable by a consensus of best medical opinion.[2] According to this consensus, the proportion of successful results for accessible sites—skin, uterus, rectum, and female breast, for example—could reach 70 to 95 per cent if cases were diagnosed and treated early enough.

The latest series of cancer morbidity surveys in ten metropolitan areas conducted by the National Cancer Institute revealed that two-fifths of the cases among males and three-fifths among females involved primary sites accessible to direct examination.[4] The relative importance of these sites is indicated in Fig. 1. Ninety-five per cent of the skin cases were diagnosed while localized. A perhaps more surprising feature is the low proportion of localized cases for the other accessible sites. Excluding skin cancers, only 50 per cent of accessible

cancers were diagnosed early. In cancer of the breast, a highly accessible site, only two of every five cases were diagnosed while localized. For cancer of the rectum, the proportion is less than one-half; for prostate, one-half; and for uterus, less than three out of five. Available data suggest that these distributions by stage and site have remained stable for several years. While these data are influenced both by patient delay and tumor grade, factors not controllable by the physician, there is little doubt that many more cases could be found in the localized stage if physicians heightened their index of suspicion. The methods of examination for cancer are, basically, a case history, direct visualization or palpation, selected diagnostic tests when indicated by the first two methods, and biopsy for confirmation of diagnosis.

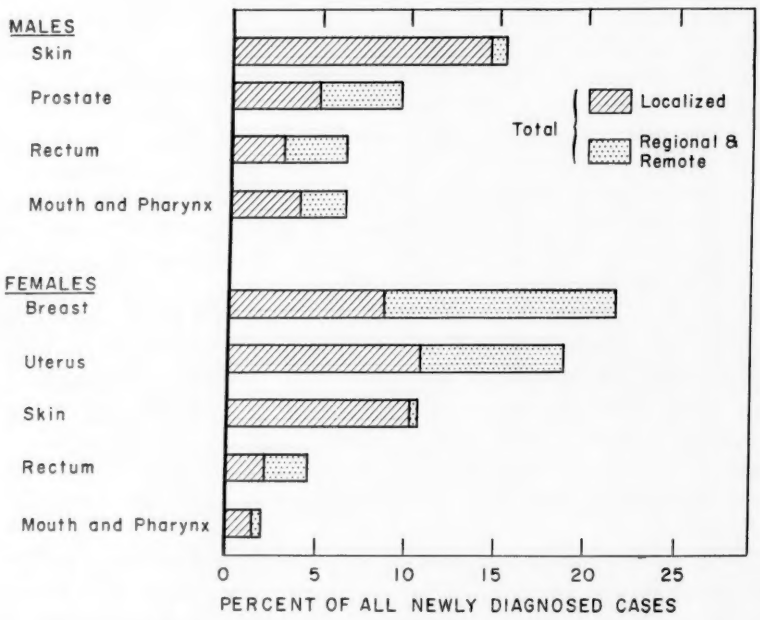

Fig. 1.—Accessible sites by frequency of diagnosis.

One cannot expect that increased diagnostic efforts will be equally productive for each site in terms of lives saved. The possible contrast in this regard between the two leading, and accessible, female sites—breast and uterus—may be pertinent. Breast cancer represents about one-fifth of all accessible cancers. Many breast cancers are found by women themselves, but in various stages of tumor development. Despite efforts to educate women in breast self-examination and to encourage doctors to include breast examination in routine medical checks, cancer morbidity data have shown no improvement in the proportion of breast cancers detected while localized. Nor has there been any marked shift in breast cancer mortality. A large-scale field test on the showing of a breast self-examination film has been undertaken in Iowa.[5] The results of this

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effort cannot be evaluated yet. If trials in Iowa and elsewhere prove negative, however, new approaches must be tried, including such possibilities as cytologic examination of breast secretions.

The uterus represents almost 20 per cent of all accessible cancers. There is increasing evidence that vaginal cytology picks up unsuspected, asymptomatic cervical cancer and that the proportion of cases diagnosed while localized is growing. A study is under way in Memphis to determine if this is a feasible public health activity for the control of invasive uterine cancers. Early indications promise that this may be an effective livesaving measure. The time may be approaching when every physician will consider vaginal cytology as part of a routine examination for women over 25 years of age.

Cancer of the mouth and pharynx constitutes over 6 per cent of the accessible cancers among men and about 2 per cent among women. These areas are easily checked. More than half of all rectal cancers are within palpable digital reach or proctoscopic check. The markedly better treatment results for localized cases in these sites, as opposed to those with metastases, assures that these physical checks will be productive. One characteristic of the accessible sites is the good treatment results for cases diagnosed early. The best dividends in lives saved can be expected from concentration in that area.

This does not mean that efforts directed to the more inaccessible sites should be neglected, even if less productive. Cancer of these inaccessible sites may be first suspected by a family doctor. Such sites as large intestine show good survival experience for localized cases. Complaints of gastrointestinal disturbances should be checked by fluoroscopy, x-ray, proctoscopy, and cytologic examination of appropriate specimens. Many problems remain to be overcome, such as those typified by such sites as stomach and lung and bronchus. The over-all five year survival rate for gastric cancer is not better than 5 per cent;[6] even for cases diagnosed early, the results are very unfavorable. The Mayo Clinic has reported a favorable five-year survival experience of 49 per cent for a series of cases without metastases,[7] but this may reflect the influence of low-grade tumor growth and possibly cannot be duplicated for all early cases uncovered through greater diagnostic effort. For lung cancer a similar situation prevails. Even for localized cases the survival rate has been extremely low, 6 per cent.[8] The early discovery of lung cancer by such measures as routine x-rays and cytologic examination of sputum does not improve prognosis to the same degree as for other sites. While we must do the best we can with measures at hand, we must look for more promising diagnostic, therapeutic, and preventive measures.

One hopeful sign is the development of basic cancer register data in some health departments and hospitals, the latter being spurred by the American College of Surgeons' program for the accreditation of tumor clinics. These will permit evaluation of the results of collective efforts to diagnose and treat cases at an earlier stage. One past difficulty has been that physicians have had little basis other than clinical impressions to judge the effects of their efforts. As more concrete statistical evidence is accumulated, physicians should be

stimulated to continuous reappraisal of their examination procedures and to select and emphasize those activities proved most productive for the detection of cases in a localized stage.

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FATIGUE

Vagueness in the application of the term *fatigue* has limited its usefulness in clinical medicine. This is unfortunate because the basic physiologic facts, properly applied, can enhance our understanding of disease processes. Use of the word *fatigue*, on the other hand, to describe all sorts of feelings of ill health on the part of patients can result only in the perpetuation of inexact thinking.

In the study of isolated tissues, fatigue is manifested by a decrease in the ability to perform work. In some cases, this is related to decrease in the availability of oxygen and combustible material to carry on the increased metabolism of work. In other cases, there would seem to be an internal exhaustion of other elements in the metabolism which is understood less clearly. In muscular tissue, there is also an accumulation of acid end products of metabolism which contributes to the loss of function and therefore to fatigue.

In studies of the total organism, it is proper to apply the same criteria, although perhaps less exactly, and to emphasize the decreased capacity to perform work rather than the merely subjective sensations arising after work. Weakness and aching pain in calf muscles on climbing stairs are subjective sensations, but, if accompanied by rapid onset of dyspnea and forced slowing of pace or stopping, they acquire increased significance as symptoms of fatigue. Experience has shown that the subjective sensation may simulate fatigue rather than truly indicate it. Even work experiments on dogs have shown that simulated fatigue is common.

The manifestation of physical fatigue in the total organism must be due to a breakdown in one of the chain of events necessary for activity. Most commonly, in normal individuals and also probably in most disease states, fatigue is caused by an inadequate circulation to the working part. If the failure is the inability to enhance cardiac output adequately, the manifestations will be primarily cardiopulmonary, i.e., dyspnea and generalized weakness. Increased heart rate out of proportion to the severity of the exercise likewise often indicates an inadequate cardiac output. If the circulatory failure is local, there will be weakness and aching of the muscles, a common example of which is the failing legs of the "aging" athlete or worker.

Less common, but nonetheless important, are the local manifestations of fatigue, such as when a small group of muscles is called upon to do excessive work. We often experience this in hand grip when called upon to carry a heavy suitcase. Here, unlike the situation in the nerve-muscle preparation, the block to further contraction is probably not primarily in the peripheral nerve or in the muscle, but is rather at one of the synapses along the path from the cortex. The adequacy of the peripheral mechanism can be proved by the response to peripheral stimulation of a completely fatigued muscle.

Fatigue in the peripheral neuromuscular apparatus is probably limited to instances of peripheral muscle disease or peripheral circulatory block. There is, of course, in addition, the special case of fatigue caused by block at the neuromuscular junction in myasthenia gravis.

It can be seen from the above description that fatigue in a physiologic sense is not readily applicable to the patient at rest. Chronic fatigue in a clincal sense must refer either to easy fatigability on exertion or to delayed recovery from fatigue after exertion. Obviously, the clinical symptoms of fatigue can be interpreted only if the degree of activity or other stress and the time relationship of the fatigue syndrome to the exertion are known.

Since fatigue as a sensation of the patient is readily simulated by other processes, it is important to confirm the impression of easy fatigability or persistent fatigue by detecting the signs of abnormal circulatory stress or signs in other systems. Physical signs and laboratory tests must confirm whether the fatigue manifestation is due to primary circulatory disease, to anemia or other blood disease, to endocrine disturbance, to primary chemical or metabolic derangement, or to disorders of neurologic control of muscles.

Before turning to the other commonly described types of fatigue, it would be well to interpose a word about physical conditioning, since the principles involved in this process are crucial in devising therapeutic programs to combat easy fatigability when it is on a genuinely physical basis. Inactivity from any cause leads to decrease in physical capacity of the muscular system, by reducing both the size of the muscles and their circulation, and also by reducing the ability of the circulatory system to increase muscle circulation readily on demand. Illness is one special form of inactivity, the effects of which are especially rapid and intense in reducing the capacity and adaptability of the muscular and circulatory systems. This deconditioning following inactivity or illness does not spontaneously reverse itself. As far as we know, the only means of reachieving increased capacity for muscular effort is by doing muscular work. Furthermore, the work must be sufficiently strenuous to induce fatigue, particularly if better circulation of working muscles is desired. Practically, it is obvious, therefore, that a program of rapid convalescence must allow for certain periods of activity to induce moderate fatigue, for adequate rest to recover from the fatigue, and for increasing strenuousness as the program proceeds.

Fatigue is not necessarily an undesirable symptom. It is necessary in any program to enhance physical performance, and, if properly interpreted, it is useful as an index of the degree of stress which activity imposes. From a teleologic point of view, fatigue might be considered a useful brake which prevents the continuance of harmful excesses of activity.

Physiologic and industrial experiences tend to indicate that physical fatigue is harmful in normal individuals only when it is cumulative. Cumulation of fatigue can be prevented on a short-term basis by a rest period or a night's sleep. Figures on industrial production suggest also that fatigue may be cumulative over longer periods of time, in which case a week-end break in strenuous industrial work, or a summer holiday, may restore the individual to his previous capacity.

Unfortunately, most of our basic knowledge of fatigue has been obtained from young individuals. The decrease in capacity for physical exertion which occurs with age is imperfectly understood. What is known is that the capacity of the local muscle circulation to increase becomes impaired with age. Furthermore, it is an established fact that maximum cardiac output begins to fall off even before the age of 30 years.

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It would be fortunate for the clinican if fatigue were wholly limited to the physical manifestations so far discussed. Clinically, it is probably much more common to find the complaint of fatigue which is not related obviously to decreased physical capacity. Commonly, the terms "mental" and "nervous" fatigue are used to describe these other forms of fatigue. Of these two, genuine mental fatigue is probably the less common. It is the type of fatigue occasionally observed after intense mental effort under nondisturbing conditions; for example, after prolonged reading or mathematical calculation. No metabolic explanation has been demonstrated to explain the mental dulling which occurs after purely intellectual activity. Almost all isolated neurologic mechanisms seem to have much greater capacity than is taxed by any fatigue situation in the intact organism.

The fatigue of most sedentary workers is probably not mental fatigue, but falls into the class which has been called "nervous" or psychologic fatigue. The executive working under high tension, the frustrated office or factory worker, or the disinterested student, is probably not overtaxing his mental or his motor apparatus. We see striking local manifestations of this form of fatigue in the several syndromes related to "writer's cramp," in all of which the uncomfortable symptoms are brought on not by the use of specific muscles but by the performance of certain psychologically significant tasks. When the symptoms are more general they may be lethargy, muscular discomfort, mild depression; frequently, they appear upon mere contemplation of an uninspiring task. In some cases, the sense of fatigue and disinclination to carry on are probably manifestations of simple boredom. Usually, however, this would appear to be more complex. In an industrial setting, the Hawthorne Study* by Mayo has furnished an example of how complex are the factors which affect work output and how overwhelmingly great are the psychologic factors affecting morale and satisfactory interpersonal relations among the working group.

The recent emphasis on pituitary and adrenal mechanisms in the explanations of responses to stress is of great importance to the subject. Further clarification is necessary, however, to tie these mechanisms to the symptomatology of fatigue. Furthermore, fatigue is encountered in situations in which the stress is probably too meager to induce major endocrine effects.

If fatigue is to become a more useful concept in clinical medicine, the manner of its induction must be explicitly determined for the individual patient. Fatigue, unqualified, means nothing. If its physical manifestations are pain, dyspnea, muscular weakness or cramps, they have as symptoms the usual significance in themselves. If fatigue is related to physical exertion, the degree of exertion should be noted and, if possible, directly observed. If fatigue is not related to physical exertion, the nature of the stress causing it is the prime diagnostic clue.

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*Mayo, Elton: **Human Problems of an Industrial Civilization.**

APHASIA

Earlier this year, Sir Winston Churchill, while still Prime Minister, disclosed in a House of Commons debate that, two years ago, he "was struck down by a very sudden illness which paralyzed me completely physically."

Although at the time there had been many rumors as to the nature of his illness, it was officially said that Sir Winston had retired for a month of rest. From his own statement and other reports, it may now logically be concluded that Britain's 80-year-old Prime Minister suffered a stroke, with the typical sequelae of paralysis of one side of the body and aphasia.

Both the rapidity and extent of his recovery are encouraging to the estimated 1,800,000 persons in the United States who have been similarly affected.

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Because of Sir Winston's great rhetorical ability, which has obviously returned, this is especially true for those with aphasia, one of the most poorly managed medical problems, both diagnostically and therapeutically.

The loss of communication as a result of aphasia causes deep emotional stress and great frustration to the patient. It is frequently misunderstood by family and friends, who may misinterpret it as a sign of mental deterioration. This, however, is not necessarily the case, for aphasia itself is a motor or sensory disturbance and has no effect on the ability to think or to reason.

The aphasia patient has lost the ability to associate symbols with actual objects or meanings. This does not mean that he does not recognize the object, its characteristics, and its uses, but rather that he is unable to associate the correct word symbol with the object or with a thought he wishes to express.

A similar situation has occurred to most of us many times. We suddenly meet a friend whom we have known for years, but are unable momentarily to recall his name when we attempt to introduce him. Multiply this embarrassing experience by a thousand such situations a day and one may comprehend the problems of the aphasia patient.

If the brain damage is temporary and minimal, there is usually spontaneous recovery within a relatively short period. Such was undoubtedly the case with Sir Winston, who resumed his official duties in a month.

If the damage is permanent, however, a lengthy and painstaking period of retraining by a speech therapist is necessary. The process is frequently slow, but substantial improvement can be made, especially if the family and friends understand the problem and participate in the retraining.

The best results can, of course, be expected when the retraining is conducted by a skilled, experienced speech therapist who is concerned with the pathology of speech and, as a professional worker, evaluates, diagnoses, and treats speech

disorders. Physicians can obtain the names of qualified speech therapists in their areas from the American Speech and Hearing Association.*

If a trained speech therapist is not available, successful retraining can be given by a teacher, friend, or the family. Taylor and Marks have recently published a *Manual and Workbook: Aphasia Rehabilitation*,† particularly designed for home use by the families of aphasic patients.

A dynamic approach to the total needs of the aphasic patient pays real therapeutic dividends.

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†Taylor, Martha L., and Mark, Morton, M.D.: Aphasia Rehabilitation: Manual and Workbook. New York, Institute of Physical Medicine and Rehabilitation, 400 East 34th Street, $3.00.

THE ROLE OF RESEARCH IN THE CONTROL OF VENEREAL DISEASE, PAST, PRESENT, AND FUTURE

In April, 1955, there was held in Washington, under the joint auspices of the United States Public Health Service and the American Venereal Disease Association, the Annual Symposium on "Recent Advances in the Study of Venereal Diseases." I was assigned the task of speaking on the topic represented by the title of this editorial.

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My initial dismayed reaction was that if venereal diseases had in fact been controlled, research and its application had had little or nothing to do with it. Second and more sober thought not only prompted a revision of this discouraging thought, but also suggested that research in "venereal disease" had had implications for medical science far beyond venereal diseases themselves. At about this early point in preparation of a manuscript, I was fortunate enough to rediscover and reread Flexner's famous address on "The Usefulness of Useless Knowledge",[1] reprinted in full in this issue of the JOURNAL. Flexner's thesis prompted the following discussion, since it was at once clear that research, apparently temporarily useless in syphilis control, had had widespread usefulness for medicine as a whole.

The too-inclusive title assigned me should perhaps be simplified by its limitation to syphilis. This is the only venereal disease which, so far as I am aware, gives any sign of having been even partially controlled. There is no clear-cut evidence that any dent has been made in gonorrhea. It may be that there has been some reduction in the number of *persons* who acquire gonorrhea in a given time period; but there is no evidence that the number of fresh *infections* has decreased in the least. In other words, in prechemotherapy days, one individual might acquire gonorrhea once or twice a lifetime; now he can acquire it once or twice a week. As to granuloma inguinale and lymphogranuloma venereum, it is true that the incidence of these infections has decreased, but no one knows why, since no one knows even elementary facts about their epidemiology. Chancroid is a regional disease, decreasing in one area with improved sanitation, unchanged in incidence in another slightly more uncleanly population group.

As to syphilis, the most fascinating of the venereal infections, there is no doubt of two "control" facts: that the incidence of fresh infections has shown a constantly decreasing trend in this country and Western Europe for 100 years or more; and that the fall in incidence has been greatly accelerated in the past ten years. These are the facts which the enquiring mind must, if it can, relate to the role of research in bringing them about.

It is pertinent to examine the great discoveries of research in syphilis, particularly so because 1954 was the centennial of the birth of Paul Ehrlich, and 1955 the semicentennial of the discovery of *T. pallidum* by Schaudinn and Hoffmann.

For more than 400 years after syphilis first became a major problem, research was slow, halting, and wholly clinical in character. Many important clinical observations were made, culminating in the monumental studies of Alfred Fournier in the last half of the nineteenth century. It is desirable to remind a modern audience of this great clinician and his work. Many a more recent syphilologist, believing himself to have discovered a new clinicial entity due to syphilis, has been chagrinned to find that Fournier had described the same entity in full and ample detail from 50 to 100 years before. But these clinical studies, valuable as otherwise they were, contributed little or nothing to the control of syphilis.

The real flowering of research in syphilis covers a brief forty-eight year period, 1901 to 1949. The outstanding accomplishments were:

1901. The discovery of the phenomenon of complement fixation by Bordet and Gengou.

1903. The transmission of syphilis to experimental animals by Metschnikoff and Roux.

1905. The demonstration of *T. pallidum* as the causative agent of syphilis by Schaudinn and Hoffmann.

1906. The application of the Bordet-Gengou complement fixation phenomenon to the laboratory diagnosis of syphilis by Wassermann, Neisser, and Bruck.

1907. Fundamental studies of Michaelis leading to present-day flocculation tests.

1907-1910. The first effective chemotherapy of syphilis—salvarsan (606), developed by Ehrlich in 1907, and applied to syphilis by Ehrlich and Hata in 1909.

1917. Wagner von Jauregg's malaria treatment of general paresis.

1921. The introduction by Sazerac and Levaditi (following the neglected suggestion of five years earlier by Sauton and Robert) of bismuth into the treatment of syphilis.

1928. The discovery of penicillin by Fleming.

1936. The immortality of *T. pallidum* at −70 degrees C., first shown by Turner.

1940. The demonstration by Florey and his associates, of the antimicrobial activity of penicillin in man.

1943. The usefulness of penicillin in the treatment of syphilis, first shown by Mahoney, Arnold, and Morris.

1949. The treponemal immobilization (T.P.I.) test of Nelson and Mayer, preceded ten years earlier by Turner's demonstration of protective antibodies in the serum of syphilitic rabbits.

What effect had these fundamental discoveries on the control of syphilis? They steadily improved the diagnosis of syphilis and its treatment; they made possible experimental study of the biology of the infection and such basic contributions as those of Chesney and his associates on immunity; but at least for forty-five years—1901 to 1946—they accomplished not one small ripple in syphilis control. True enough, the incidence of syphilis declined over all (with major upward fluctuations punctuating its fall) during these forty-six years; but the decline had been going on for forty-six or more years before 1901, at a time when none of this present-day knowledge was available, and before there was any organized effort of any kind at control. Moreover, the rate of decline in the first half of the present century was (allowing for jogs due to war or population unrest) nearly a straight-line continuation of that of the last half of the nineteenth century.

This earlier but none the less significant decline is certainly related to a similar epidemiologic experience with the other major chronic infection of civilization, tuberculosis. The morbidity and mortality of this scourge has also been steadily falling for more than a century, a fall initiated, as with syphilis, before the great scientific discoveries of etiology, methods of spread, etc., and before any organized control efforts were available. It is possible, but hardly probable, that these parallel declines in incidence of syphilis and tuberculosis were due to increasing racial immunity. Much more likely were they caused by the common factor of improved standards of living, and sanitation, brought about by the industrial revolution. Exacerbation epidemics of both infections have punctuated the rates of decline of each; and those, as I have shown in the Malcolm Morris lecture in 1950,[2] are clearly related in all countries to the population instability brought about by wars, revolutions, and political unrest.

The abrupt increase in downward trend the last few years in the morbidity of both infections is, however, probably due to another factor—the advent of antibiotics. The great scientific discoveries in each infection—in syphilis, the basic contributions of 1901 to 1928—may be regarded as having been locked within the strong and impermeable casing of an atomic warhead. No one of these discoveries, alone or in combination with others, could in themselves explode the bomb and release the benevolent forces imprisoned therein. As with the fusion bomb, a fission trigger was needed to burst the casing. That trigger was provided, for syphilis by penicillin, for tuberculosis by streptomycin, PASA, and isoniazid. Once released, all the favorable factors involved in experimental studies, improved diagnosis, and public health control measures could come into full play, and apparently they have done just that.

As to the great fundamental research advances in syphilis, it is quite certain that they have proved in the long run to be of much more value to medicine in general than to the control of syphilis in particular. The immunologic groundwork of Bordet and Gengou, Wassermann and his collaborators, and Michaelis has provided a diagnostic approach to infectious disease in general, whether acute or chronic. Perhaps even more important, they are an early part of the

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science of immunochemistry in general, and offer the groundwork of the yet to be accomplished study of tissue damage by noxious antigens in noninfectious chronic illness.

Turner's observation of the humoral nature of immunity in syphilis at once placed this infection in its proper place as a member of the group of infectious diseases in general, instead of in a bizarre, peculiar, and isolated position of microbial grandeur.

The application of Turner's fundamental contribution to the TPI test by Nelson and Mayer has clarified diagnostic confusion as to the phenomenon of biologic false positivity, and has opened up a fascinating new avenue of approach to the study of noninfectious collagen vascular disease.

Metschnikoff and Roux made possible the later important studies of Brown and Pearce, Chesney, Turner, and Eagle (to mention only a few of those who have labored with the experimental biology of syphilis and other treponematoses).

Schaudinn and Hoffmann unlocked the microbiologic door of all spirochetal and treponemal diseases of man and animals.

Ehrlich was of course the father of modern chemotherapy, responsible in a sense for all who have followed him in this field, and for important fundamental studies in such collateral phases as drug resistance and drug sensitization.

Wagner von Jauregg was perhaps the first to point out that fever was a desirable rather than an undesirable consequence of infection (e.g., as in typhoid fever) and that nonspecific methods of treatment could, in certain types of syphilis, accomplish more than treponeme-killing drugs. Indeed, he was the first to transform a completely fatal infection—paresis—into a curable disease.

Turner's discovery of the indefinite viability of *T. pallium* at cold temperatures is now an everyday tool to all microbiologists in all infections. In a sense, it has played a great role in the recent major vaccinial victory over poliomyelitis; and may eventually influence even the geneticists, since sperm cells too are apparently immortal if sufficiently cooled off.

As to Fleming, he is in essence and single handedly responsible for the control of all microbial disease.

So far I have been able to speak only—and then far too briefly—of nine great and four subsidiary research discoveries in syphilis. Of these, the two which eventually proved to be of most importance to syphilis—those of Bordet and Gengou and of Fleming—were made without thought of syphilis in the minds of the investigators; and each of them has been proved of great and enduring worth to all of medicine.

From the public health point of view, it is difficult, if not impossible, to appraise the effect on venereal disease control, and specifically on syphilis control, of the mass application of public health methods or of individual components thereof. It seems a reasonable statement that no public health effort in this country or elsewhere has successfully modified human behavior. The vector of venereal disease is man himself, and the act by which it is usually transmitted is that of sexual intercourse. While there are no accurate biostatistical studies

(other than those of Kinsey) defining the frequency of sexual intercourse in various countries and in various areas, it seems likely that by and large there is about as much sexual contact now as there was 50,000 years ago or at any other time in the history of mankind.

The major contribution of public health control measures would seem to be in case finding by means of serologic surveys and by "shoe leather epidemiology."

Public health workers have, however, played another very important role in developing cooperative effort between physicians and groups of physicians in the evaluation of treatment results and other factors, and in developing the biostatistical methodology of such studies. In sequence, one may point to the several studies of the League of Nations and of the World Health Organization on an international basis, and of the United States through the nationwide study of the penicillin treatment of early syphilis sponsored originally by the Committee on Medical Research and later by the United States Public Health Service. These studies have enlisted the interest and aid of competent biostatisticians. Each of them has been progressively better, avoiding the biostatistical errors of its predecessors.

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These studies dealt primarily with the relatively simple problem of evaluation of treatment in early syphilis. Extension of these into the field of late syphilis, as exemplified by the Johns Hopkins-Cornell-University of Pittsburgh studies of the natural history of cardiovascular syphilis and the current cooperative effort of a number of universities with the United States Public Health Service in the treatment of neurosyphilis, has begun to set a pattern of medical clinical investigative effort with biostatistical cooperation, which is applicable to a study of the natural history of chronic disease as a whole. There is a growing awareness, for example, that one cannot evaluate the results of surgical and medical procedures in the treatment of so common a condition as essential hypertension, without basic information of what appears in the absence of such treatment. As a result of such studies, it has become clear that the enormous medical literature with respect to the treatment of this, that, and the other chronic condition, for example cardiovascular syphilis, is practically worthless for lack of proper controls. A future investigator who plans an evaluation of treatment procedures must inevitably be influenced, directly or indirectly, by the groundwork of those who have struggled with the problems of syphilis.

Finally, from the extent to which syphilis may have been controlled by research may be drawn analogies applicable to chronic disease in general; and a fresh example of this has just been given by the new poliomyelitis vaccine. The culminating development of this vaccine stood on a foundation of painstaking, snail-like medical progress by a large number of investigators, all of whom were consciously or unconsciously influenced by their predecessors. The credit belongs not to one person, but to hundreds of patient, tireless people, of this or earlier generations, each of whom deserves a share of the credit which is so generously lavished on the winner of the jackpot.

The pattern of syphilis research may be expected to be duplicated also in another respect, namely, that basic discovery may follow basic discovery in a given field, for example, arteriosclerosis; each of these discoveries alone or in combination with others is relatively useless in control until finally another investigator, like Fleming, working in a totally unrelated field, finds the key which unlocks the safe and releases for the benefit of mankind all of the basic work which has gone before, amalgamating it into a unified whole.

Future advances in venereal disease control cannot even be imagined. They may well lie in the hands of the inquiring microbiologist, who, uninterested in venereal disease as such, is nevertheless stimulated by his own intellectual curiosity to attempt an unraveling of the myriad of unsolved biologic problems which, in spite of penicillin, we still face.

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Book Reviews

THE PHARMACOLOGICAL BASIS OF THERAPEUTICS. By Louis S. Goodman, M.A., M.D., and Alfred Gilman, Ph.D., Ed. 2. Pp. 1831. New York, 1955, The Macmillan Company. Price $17.50.

The first edition of the book written by Goodman and Gilman was a phenomenal success. Students and practitioners found it readable and dependable; most teachers felt no qualms about recommending it as a text. Fourteen years have elapsed since then, and the absence of a new edition has been sorely felt, particularly since a completely satisfactory substitute has not been available. At last, however, these two authors have brought their book up to date and presented it to the profession for inspection.

To set the review in the proper tone, one ought to begin with accolades. For any two men to cover the field of pharmacology and therapeutics in even a *moderately* thorough fashion is no mean task. The exhaustive job which Drs. Goodman and Gilman have done is awe-inspiring. It is hard to think of major articles whose existence has eluded the authors, and most of the references (major and minor) have been beautifully abstracted. The experience and talents of Drs. Goodman and Gilman enable them to keep calm heads in the face of optimistic and enthusiastic claims for new drugs, and new work on older drugs has for the most part been neatly synthesized into the previously available text. The familiar and literate style of the old edition is maintained, and new chapters and sections have been added to insure completeness.

Although it may seem ungracious to carp, in view of the above blessings, a few criticisms seem in order. The very completeness of the book has made it large and cumbersome (1831 pages). The attempt to put some of the less vital details in small print results in numerous sequences with entire pages in unpleasantly small type following one upon the other. The massiveness of the book makes it almost ridiculous to term it a textbook. It is rather an encyclopedia of pharmacology, and therefore less than perfect for use in an undergraduate course. (Perhaps the authors will consider writing an abridged version entitled "A Guide to Goodman and Gilman for the Perplexed".)

At times one wishes that the authors had abandoned their Olympian detachment toward conflicting data, and forsaken the middle-of-the-road view for a critical stand, or even omitted the more dubious side of a particular controversy. There are also occasional statements purporting to be fact which are a little unnerving to this reviewer: "A knowledge of the basic mechanism of action of a drug invariably leads to its more effective therapeutic application." "Most drugs . . . affect only a specific tissue or group of receptor cells." "The study of the relationship between chemical structure and pharmacological action . . . has led to the synthesis of many valuable therapeutic agents." "Drug fever is a hypersensitivity phenomenon that very closely resembles serum sickness and is manifested by fever, leucocytosis, arthralgia, and skin reations." "It is much easier to correct anesthesia which is too deep than anesthesia which is too light." There is an arbitrary classification (on what data?) of barbiturates into drugs lasting "under 3 hours, 3-6 hours, and 6 or more hours." "The barbiturates are not analgesics, but they do alter the perceptual and emotional responses to pain." "The data obtained from laboratory experiments (von Frey hair analgesic technic) . . . are of importance to the physician in his selection of opiates." "Hypersensitivity to pain after analgesia has worn off is nearly always noted." "Meperidine has the obvious advantage over opiates of not causing respiratory depression. . . ." et cetera. Although everyone will be able to find some statements with which he does not agree, it should be emphasized that errors are comparatively rare—astonishingly infrequent considering the scope of the text.

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Despite certain reservations (price could be included here), the good qualities of this book so outbalance the bad that it can be heartily recommended to students and physicians. The text will probably remain the definitive one in the field until a good many years have elapsed (or until Goodman and Gilman write another edition).

Louis Lasagna

A History of Medicine. By Ralph H. Major, M.D. Two volumes. Pp. 1155, with 262 figures; indexed. Springfield, Illinois, 1954, Charles C Thomas. Price $14.50.

This newest history of medicine is the story of the art of healing from the dawn of man's existence to the middle of this century. It is readable without being dramatic, and it is beautifully and richly illustrated. Each chapter is followed by "Biographical Addenda," containing short passages on those personalities who had to be excluded from the text because of lack of space. Of particular interest is the last chapter on the twentieth century which has so far not often been included in historical works. The list of Nobel Prize winners in medicine and physiology is also very useful.

In the preface to his book Dr. Major himself has anticipated most of the criticism with which reviewers might receive his work. He stresses that lack of space made it necessary to treat many aspects and personalities cursorily or to leave them out altogether; and his bibliography and acknowledgment confirm his statement to the effect that much of his work is based on secondary rather than on primary source material. Dr. Major intimates that his *History of Medicine* adds little to the ones already in existence, and he points out that it "is not written for the specialist in medical history, to whom most of the facts related are already well known," but for the medical student and practitioner in the hope of arousing in them a greater interest in the history of their profession. With Dr. Major's objectives and reservations in mind, the volumes here reviewed have considerable merit. To the nonspecialist and the novice in the field, they will serve as a comprehensive and instructive introduction to the history of medicine.

Ilza Veith

Medical Mycology. By R. D. G. Simons, Ph.D., Pp. 446, with 257 figures; indexed. Houston, Texas, 1954, Elsevier Press. Price $9.75.

In a book such as this in which thirty-six authors from many different countries have contributed one or more chapters, it is impossible to criticize each subject separately. However, some of the more significant contributions may be singled out for comment. The introductory chapter by Emmons gives a good review of the chief problems concerned in any study of mycotic infections. That of Simons and Gohar on classification and nomenclature is also well done, and includes excellent illustrations of many of the pathogenic forms. In a section written by Reiss on experimental infections, the data regarding methods and susceptible animals are covered in a concise manner, providing a ready reference source for anyone working on this particular phase of the subject.

Some of the conditions that seem especially well described are coccidioidomycosis, histoplasmosis, epidermophytosis, sporotrichosis, moniliasis, and aspergillosis. Some others, such as torulosis and the blastomycoses, are not as well covered. In the case of the latter, though the illustrations are well chosen, the few lines on therapy are definitely inadequate, with almost no mention of stilbamidine. In the chapter on actinomycosis, although there is a satisfactory description of many of the peculiarities of the local lesions, there is not much discussion of the clinical features, and that dealing with therapy seems far out-of-date.

Throughout the book the illustrations are particularly good. This obviously is a real necessity in any description of fungus diseases, as most of them are encountered relatively rarely in this country. A final chapter dealing with the cultural characteristics of many of the pathogenic fungi summarizes this phase of the problem quite well, and should be useful to anyone attempting to isolate and identify the specific organisms.

A. M. Fisher

Books Received

A HISTORY OF DERMATOLOGY IN PHILADELPHIA. By Reubin Friedman, M.D. Pp. 556; indexed, with 136 figures. Fort Pierce Beach, Florida, 1955, Froben Press, Inc. Price $10.00.

CASIMIR FUNK—PIONEER IN VITAMINS AND HORMONES. By Benjamin Harrow. Pp. 209; indexed. New York, 1955, Dodd, Mead & Company, Inc. Price $4.00.

DIFFERENTIAL DIAGNOSIS OF INTERNAL DISEASES (Clinical Analysis and Synthesis of Symptoms and Signs on Pathophysiologic Basis). By Julius Bauer, M.D., F.A.C.P. Pp. 985; indexed, with 65 figures. ed. 2. New York, 1955, Grune & Stratton, Inc. Price $15.00.

HANDBOOK OF PEDIATRICS. By Henry K. Silver, M.D., C. Henry Kempe, M.D., and Henry B. Bruyn, M.D. Pp. 548; indexed. Los Altos, Calif., 1955. Price $3.00.

VETERANS ADMINISTRATION TECHNICAL BULLETINS—SERIES 10. Vol. VII, 1954. Washington, D. C., March, 1955.

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